Newcastle Disease

Disease Monograph Series – 01

Virus | Mononegavirales | *Paramyxoviridae* | Poultry

IDRC | Bartay

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Acronyms

ACIAR	Australian Center for International Agricultural Research
AI	Avian influenza
APMV	Avian paramyxovirus
AU	African Union
AU-IBAR	African Union InterAfrican Bureau For Animal Resources
AU PANVAC	AU Pan African Veterinary Vaccine Centre
BSL-3	Biosafety level 3 (Laboratory designation required for challenge studies)
DIVA	Differentiating infected from vaccinated animals (strategy)
ELISA	Enzyme-linked immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
H	Hemagglutinin
HA	Hemagglutinin antigen
HI	Hemagglutinin inhibition
HN	Hemagglutinin-neuraminidase
I-2	Thermostable live Newcastle disease vaccine
IB	Infectious bronchitis
IBD	Infectious bursal disease
IDRC	International Development Research Centre

ILT	Infectious laryngotracheitis
HPAI	Highly pathogenic avian influenza
ICPI	Intracerebral pathogenicity index
LBM	Live bird market
LPAI	Low pathogenic avian influenza
LVIF	Livestock Vaccine Innovation Fund
MAbs	Monoclonal antibodies
NDV	Newcastle disease virus
NA	Neuraminidase
NI	Neuraminidase inhibition
NIH	National Institute of Health (U.S. Government)
OIE	World Organization for Animal Health
RT-PCR	Reverse transcription polymerase chain reaction
SEPRL	Southeast Poultry Research Laboratory (U.S. Government)
SPF	Specific pathogen free
USA	United States of America
USD/US$	United States Dollars
V4	Thermostable live Newcastle disease vaccine
VI	Virus isolation
VN	Virus neutralization
WAHID	Interface for the World Animal Health Information System
WAHIS	World Animal Health Information System (database)
WHO	World Health Organization

Executive Summary

NDV is a single stranded, double enveloped RNA virus belonging to the Order Mononegavirales, Family Paramyxoviridae [1]. The NDV is composed of 6 structural proteins: nucleocapsid protein (N); phosphoprotein (P); matrix (M); fusion (F); hemagglutinin--neuraminidase (HN); and the RNA-dependent RNA polymerase (RNAP) designated the large polymerase (L). The host protein actin, also is incorporated into virus particles and is used for virus entry [1]. NDV viruses are classified into pathotypes, with increasing severity: asymptomatic enteric based, lentogenic, mesogenic, and velogenic based on an experimental chicken challenge model. Velogenic NDV is considered by the OIE as reportable and are further characterized as either neurotropic or viscerotropic based on clinical and pathological features. Clinical signs vary depending on: virus virulence; dose; route of transmission (respiratory is fastest); host species; breed; age; host immune status (exposure and vaccination history); and other factors. A recent study assessing the F protein from 1,995 GenBank submissions revealed that class I viruses primarily affecting wild birds comprise a single genotype, while class II contains 15 genetic groups. The official incubation period of NDV defined by the OIE is 21 days however the biological incubation period is between 2-15 days, with most cases occurring within 5-6 days following exposure but possibly as long as 3-4 weeks. Species susceptibility in decreasing order are as follows: chickens, turkeys, pheasants, pigeons and ducks. The preferred method of diagnosis is virus isolation and subsequent characterization [2].

NDV is considered the most significant cause of poultry losses globally and has been reported on 6 of the 7 continents of the earth [1]. The economic impact of Newcastle disease in terms of lost livestock units between 2006-2009 was greatest in South Asia and Viet Nam [21]. Mesogenic NDV is endemic in Africa, Asia, Central and South America and the Middle East while lentogenic strains are found in all 6 inhabited continents. Wild birds are the reservoir for NDV in poultry. Commercial poultry that are vaccinated are also potential carriers of live NDV vaccine strains, which can affect smallholder populations at the interface of commercial and smallholder poultry. Velogenic NDV is endemic in areas of Mexico, Central and South America, widely spread in Asia, the Middle East and Africa, and in double-crested wild cormorants in the US and Canada [2]. From a total of 21,370 NDV events reported in 20 selected countries between 2000 and 2015, at least 5,290 (25%) NDV disease events were reported from 14 selected African countries and 16,080 (75%) NDV disease events were reported from 6 selected Asian countries. Reporting bias must be considered when interpreting these estimates. NDV mesogenic and velogenic pathotypes persist in all Asian countries.

The application of biosecurity remains challenging in smallholder settings, while marketing interventions through the value chains hold more promise to improve prevention and control of NDV. A shift away from the traditional production-based research is needed to a new approach that is market-driven and focused on trade and poverty alleviation. Including linkage with the private sector resources and skills [25]. There is no medical treatment for NDV, so vaccination remains an important means for both prevention and control of NDV in smallholder settings.

The strategic objectives for an ideal vaccine and vaccination program include the following:

- Live prime dose that is safe and non-reverting to virulent form after it has circulated in live poultry;
- Thermostable for ease of use in smallholder setting;
- Protective, long-lasting immunity resulting in reduced replication and transmission on a population basis;
- Vaccine is matched with the genotype of circulating field strains, ideally using reverse genetics technology [8][14];
- Can be delivered easily using simple and attainable field logistics;
- Rapid onset and long duration of immunity;
- Potential combination as part of a multivalent vaccine with other priority diseases for smallholders such as infectious bursal disease (IBD) based on country needs assessments.

Key Conclusions Related to Vaccination are presented as follows:

Short-term Solutions: Live, attenuated and killed, inactivated NDV vaccines are effective, and can produce protective titers when applied properly. The first approach would be to 1) improve disease detection using rapid test kits; 2) improve reporting; 3) and optimize the access and delivery of vaccines in the field since it is a limiting gap regardless of the vaccine that is used. Thermostable vaccines currently are closest to the ideal vaccine for use in smallholder poultry. Proper delivery of vaccine to smallholder with community engagement is a key gap to overcome logistical challenges for the safe and effective delivery of vaccine.

Medium-term Solutions: 1) The further development of reverse genetics vaccines antigenically matched with the field strain genotype will optimize the immune response (level and duration of immunity) in typical currently available vaccine strains. Investment in the collection and molecular analysis of country-specific field strains will be required. 2) Improvement in diagnostic tests in vitro (cell culture) and rapid tests in the field will also be needed to replace the need for SPF poultry.

Long-term Solutions: There are two main needs: 1) Further refinement of a vaccination model multivalent, non-replicating, antigenically matched and epidemiologically appropriate; 2) Development of breed lines of native poultry with high levels of innate genetic resistance to further reduce virus replication and increase vaccine efficacy.

The following gaps are highlighted in relation to vaccine development and sustainable field implementation of vaccination for Newcastle disease:

- Lack of accurate information on reservoirs as well as NDV incidence and prevalence from farmers, including epidemiologically related semi-intensive poultry producers and the government services;
- Limited genotype characterization of country-specific field strains of NDV.
- Need for field based rapid test kits to detect the field strains since no field based test kits are currently available;
- Need to replace the SPF chicken challenge based model with a cell line culture model in developing countries with laboratories lacking BSL-3 required to conduct challenge studies safely;

- Systematic delivery and monitoring of vaccine use so that it is applied uniformly among members of smallholder village flocks;
- Wider application of safe, non-replicating NDV vaccines at the interface of commercial and smallholder sectors where spillover can occur.

Clinical disease overview

Etiology

In 1926 the first reported outbreaks of Newcastle disease occurred in Java, Indonesia, and Newcastle-upon-Tyne, England (also known as peudo-fowl pest; exotic Newcastle disease; and Ranikhet disease). NDV is a single stranded, double enveloped RNA virus belonging to the Order Mononegavirales, Family Paramyxoviridae. NDV belongs to the subfamily Paramyxovirinae that includes Rubulavirus, which includes human mumps virus; Respiroviruses, containing mammalian parainfluenza 1 and 3; Morbillivirus, which includes canine distemper, rinderpest, and measles; Henipavirus, containing Nipah and Hendra virus; and the Avulavirus genus that contains NDV and other APMV [1].

NDV is a hemagglutinating virus like AI virus. The HN protein binds to host red blood cells while NA protein is associated with both entry and efficient viral release from host cells, in conjunction with F protein. Cell fusion and hemolysis is mediated by F protein, which is cleaved by host protease enzymes to form F1 and F2 by products.

There are 11 APMV serotypes, and APMV-1 is the most important for poultry, including NDV. The nomenclature for APMV is similar to the one for AI virus. A summary of APMV serotypes is presented in Table 1 [1].

Virus structure

The NDV is composed of 6 structural proteins: nucleocapsid protein (N); phosphoprotein (P); matrix (M); fusion (F); hemagglutinin--neuraminidase (HN); and the RNA-dependent RNA polymerase (RNAP) designated the large polymerase (L). The host protein actin, also is incorporated into virus particles and is used for virus entry [1].

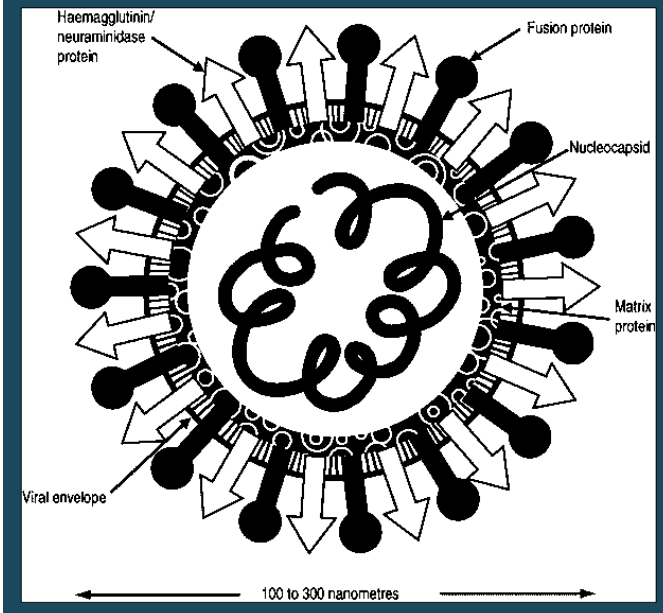


Figure 1: Schematic structural components of a Newcastle disease virion

NDV viruses are classified into pathotypes, with increasing severity: asymptomatic enteric, lentogenic, mesogenic, and velogenic based on an experimental chicken challenge model. Velogenic NDV is considered by the OIE as reportable and velogenic pathotypes are further characterized as either neurotropic or viscerotropic based on clinical and pathological features.

Newcastle disease is defined as an infection of birds caused by APMV-1 (serotype 1) as follows [1][2]:

1. The virus has an intracerebral pathogenicity index (ICPI) in day old chicks of 0.7 or greater; or
2. The virus has multiple basic amino acids (3 lysine or arginine residues between 113-116 residue positions) at the C-terminus of the F2 protein and phenylalanine at residue 117 of the N-terminus of F1 protein. The absence of basic amino acid residues also requires the ICPI test.

Table 1: Prototype avian paramyxoviruses with host range [1].

APMV group with prototype strain	Natural hosts	Other hosts	Disease
APMV-1 NDV	Many	Velogenic NDV in N. American cormorant	Mild to severe; rare in wild birds
	Pigeons (PPMV-1)	Chickens	Mild to severe
APMV-2 /chicken/California/Yucaipa/56	Turkey, passerine	Chicken, psittacine, rails	Mild; egg drop
APMV-3/turkey/Wisconsin/68	Turkey	None	Mild; egg drop
APMV-4/duck/Hong Kong/D3/75	Ducks	Geese	None known
APMV-5 /budgerigar/Japan/Kunitachi/74	Budgerigars	None known	Not in poultry
APMV-6/duck/Hong Kong/199/77	Ducks	Geese, rails, turkeys	None ducks and geese; moderate in turkeys
APMV-7/dove/Tennessee/4/75	Pigeons, doves	Turkey, ostrich	Mild in turkeys
APMV-8/goose/Delaware/1053/76	Ducks and geese	None known	Not in poultry
APMV-9/domestic duck/New York/22/78	Ducks	None known	Asymptomatic infection in ducks
APMV-10/Rock Hopper/Falkland Islands/324/2007	Rock Hopper penguin	Magellanic penguins	Not in poultry
APMV-11/Common Snipe/France/100212/2010	Common snipe	None known	Not in poultry

Epidemiology

NDV has been reported on 6 of the 7 continents of the earth. Mesogenic NDV is endemic in Africa, Asia, Central and South America and the Middle East while lentogenic strains are found in all 6 continents noted previously. Velogenic NDV is endemic in areas of Mexico, Central and South America, widely spread in Asia, the Middle East and Africa, and in double-crested wild cormorants in the US and Canada [3][4]. Between 2005 and 2015 NDV was reported to the OIE at least once in 121 countries globally [4]. Lentogenic strains of NDV are worldwide in their distribution. Mesogenic pathotypes with a special adaptation to pigeons (i.e. pigeon paramyxovirus) do not appear to infect other poultry readily [1][4]. Figures 2 and 3 demonstrate the global spatial (Figure 2) and temporal (Figure 3) distributions respective of NDV events reported either actively or passively.

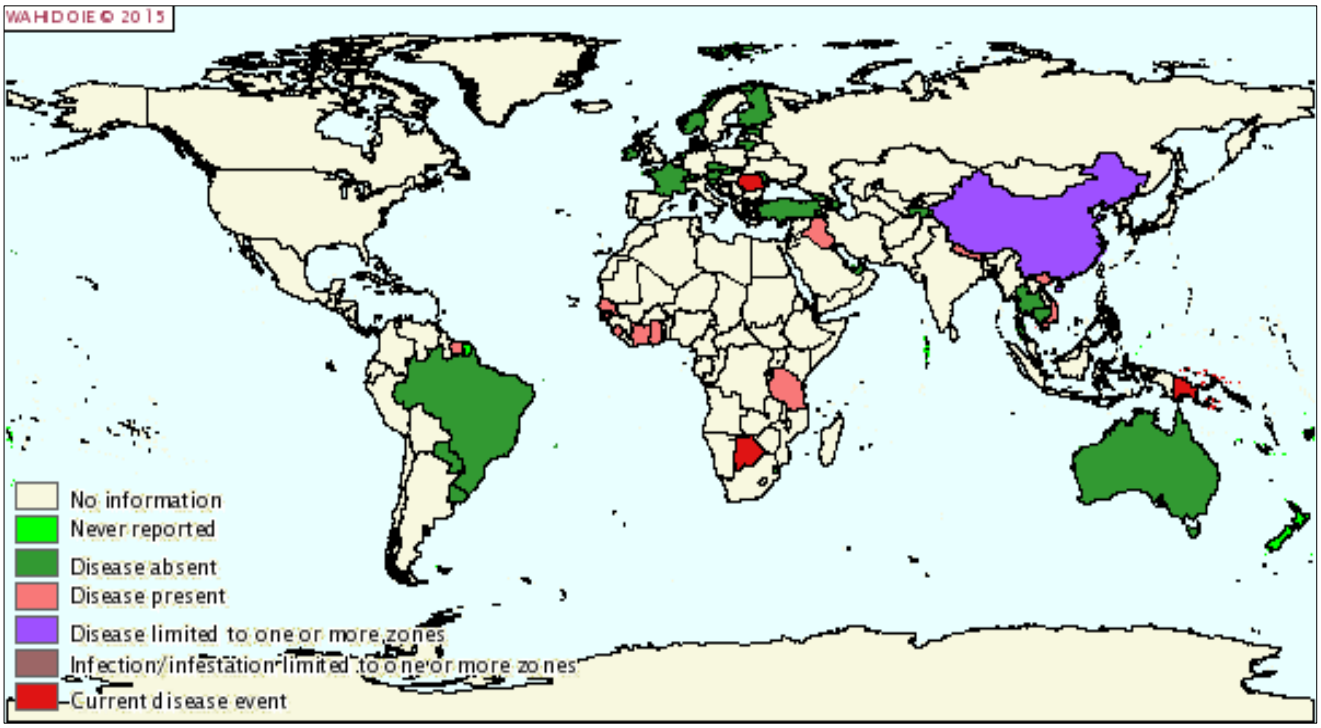
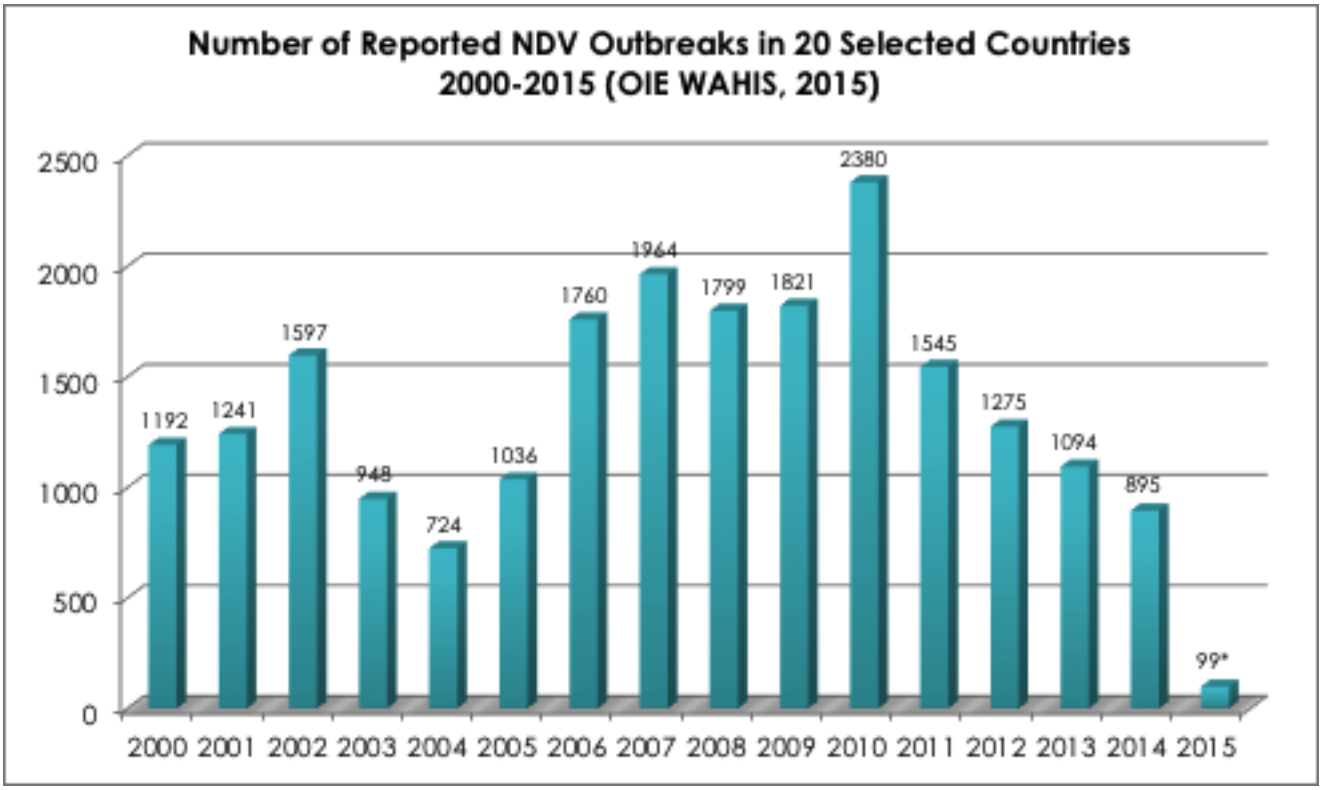


Figure 2: Spatial distribution of NDV reported in poultry in 2015 [5]



*Countries report every 6 months to OIE, hence 2015 reports are incomplete.

Figure 3: Temporal distribution of NDV outbreaks reported to OIE 2000-2015 [6]

The epidemiology of NDV is considered in terms of the epidemiological triad, including agent, host and environmental characteristics.

Agent Factors

Avirulent and virulent strains can be distinguished on the basis of the cleavage site sequence of the F protein. During replication, the fusion gene is translated into a pre-cursor protein, F0 that must be cleaved by host cell proteases into F1 and F2 subunits for the viral particles to become infectious.

APMV-1 isolates are separated into two clades, called class I and class II, based on the genetic ancestral relationship among viruses. A clade is a group of viruses linked to a common ancestor. Class I isolates have been found mainly in wild waterfowl, and are usually of low pathogenicity [7]. A recent study assessing the F protein from 1,995 GenBank submissions revealed that class I viruses comprise a single genotype, while class II contains 15 genetic groups including 10 previously established (I–IX, and XI) and five new genotypes (X, XII, XIII, XIV and XV) using a unified nomenclature and more objective criteria (Table 2) [8].

Table 2: Criteria used to define Newcastle virus genotypes based on an analysis of 1,995 GenBank submissions [8]

1	Genotype and sub-genotype designations were maintained as previously described when possible (i.e. genotype I remains I and sub-genotype Ia remains Ia)
2	New genotypes and sub-genotypes were assigned based on the phylogenetic tree topology using the Maximum Likelihood method and the optimum nucleotide model (GTR +G +I) as determined by MEGA5. Phylogenetic tree topology was supported by the evolutionary distances between groups
3	New genotypes or sub-genotypes were designated only when the complete F gene sequence of at least four independent isolates without a direct epidemiologic link (i.e. distinct outbreaks) were available
4	The mean nucleotide distance (evolutionary distances) between and within groups was inferred as base substitutions per site by averaging all sequence pairs with the MEGA5 software and the Maximum Composite Likelihood model
5	The mean interpopulational evolutionary distance (mean distance between genotypes) was estimated using the Maximum Composite Likelihood model (0.106; standard error = 0.0061) and set as the cutoff value to assign new genotypes
6	Different genotypes should have an average distance per site >10% (0.1). Different sub-genotypes should have an average distance per site between 3 (0.03) and 10% (0.1)
7	Bootstrap value at the genotype and sub-genotype defining node should be >60%

NDV demonstrate considerable drift due to transcription errors, however more recently recombination is considered to play a role in shaping the genetic structure of the APMV type 1 [7]. Progress made in recent reclassification should now be considered in relation to vaccine selection and the management of vaccination programs. The majority of NDV vaccines belong to genotypes I and II [8]. Figure 4 depicts the molecular groupings and relationships amongst the 15 NDV genotypes [8].

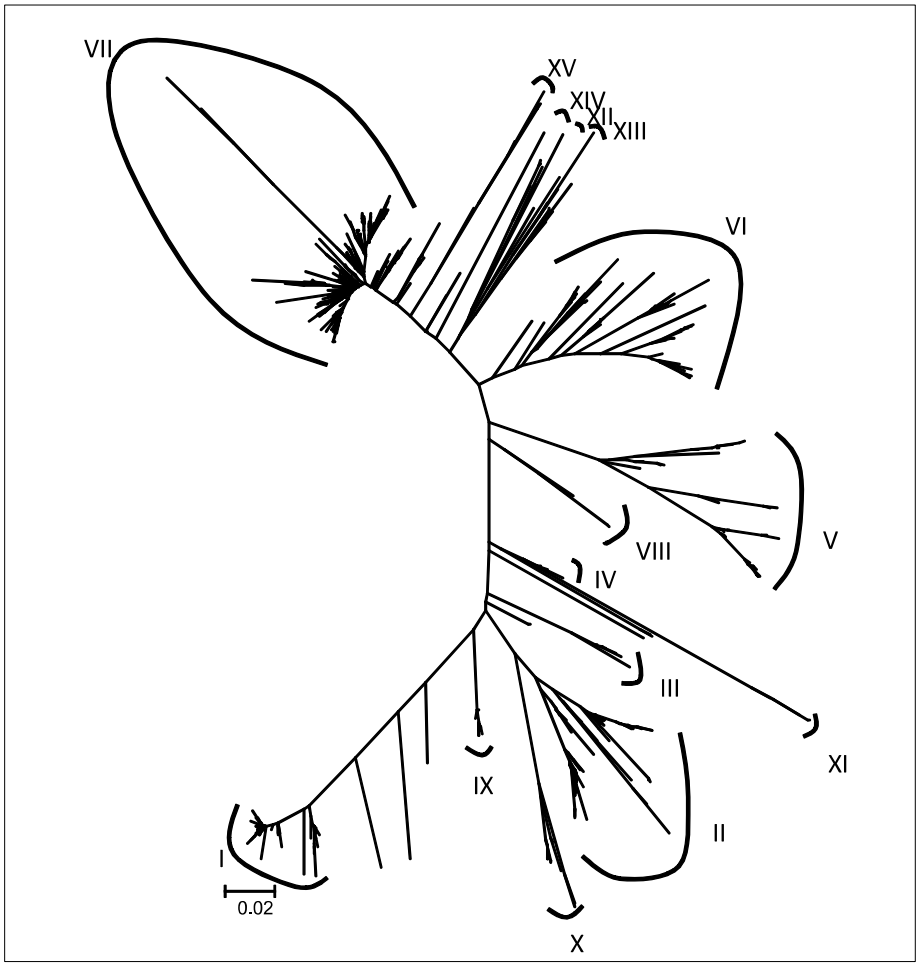


Figure 4: Phylogenetic analysis based on the complete nucleotide sequence of the F gene of viruses representing NDV class II [8]

The global diversity of NDV genotypes and among and within countries is significant. Genoptypes VII and VIII emerged in the 1960's in South Africa, Europe and Asia and genotype VII is currently the predominant genotype found in Asia [9]. Viruses characterized in Mozambique in 2005 belonged to lineage Vb, a similar finding in 1995 and can be concluded that no new introduction of the virus occurred from 1995 to 2005 in Mozambique [10]. Another recent study in Cameroon found that most strains were related to vaccine strains, but a single genotype XVII strain was also found. Only three highly similar genotype XVII strains were detected in the Central African Republic. Subgenotypes XVIIa, XVIIIa, and XVIIIb co-circulated in Côte d'Ivoire, while subgenotypes XIVa, XIVb, XVIIa, XVIIb, and XVIIIb were found in Nigeria [11]. A study conducted in Ethiopia indicated that the viruses are clustered together within the new sub-genotype VIf [12]. In Madagascar, the phylogenetic analysis of F gene from isolates resembles the "old" genotype IV but may be distant enough to constitute a new genotype, namely genotype XI (or lineage 3g) [13].

The significant genomic diversity of NDV is enhanced by the large variety of avian species susceptible to NDV infection and the availability of highly mobile wild bird reservoirs. The genomic diversity of NDV increases the possibility of diagnostic failures and unidentified infections. Therefore, ongoing epidemiological surveillance and pro-active characterization of circulating strains is required to ensure that the vaccines and PCR reagents are effectively applied worldwide. Large phylogenetic and antigenic distances between vaccines and current circulating virulent strains may facilitate the evolution of virulent/velogenic NDV [14]. Discussion of NDV pathotypes is considered below under NDV diagnosis.

Host Factors

NDV is shed from infected birds in a number of ways via: i) oropharyngeal secretions and cloacal excretions; ii) vertically transmitted through via infected eggs; and iii) inapparent (chronic) carriers (shedders) first exposed to lentogenic and/or subsequently exposed to a velogenic strains. Flies may also act as mechanical and possibly as biological vectors [7]. Transmission can then occur by direct contact with feces and respiratory discharges or by contaminated food, water, equipment, and human clothing. Humans act as ideal mechanical vectors and can be an end host with mild to severe conjunctivitis following exposure natural or vaccine strains of NDV [1][7][14].

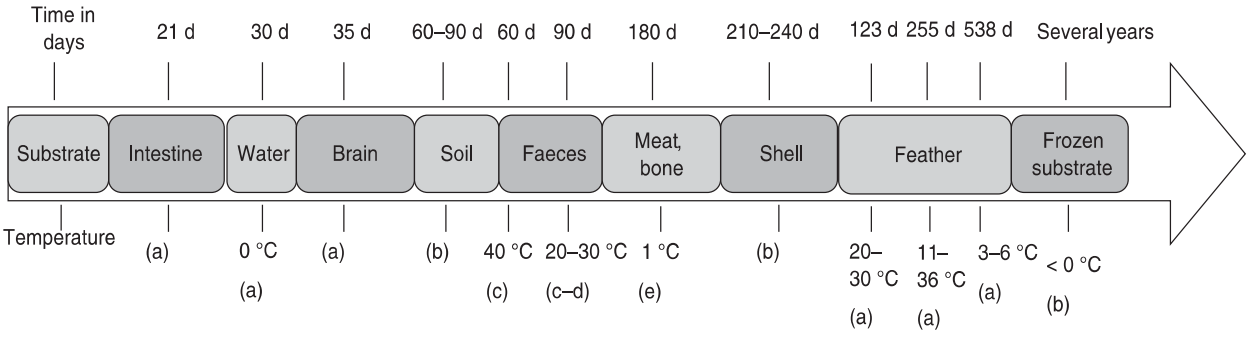
The interface between wild bird reservoirs and poultry is key to understanding the epidemiology of NDV viruses. NDV has been documented in 241 avian species [1]. Virus is shed during the incubation period and for a short time during recovery. Birds in the pigeon family can shed the virus intermittently for a year or more. Other wild birds such as cormorants have also been associated with outbreaks in domestic poultry. Wild waterfowl and shorebirds are infected with a large and diverse group of avirulent viruses that normally do not produce any clinical signs in poultry (class I). Almost half of the class I viruses found in the United States originate from the Mallard duck (Anas platyrhynchos) with six class I genotypes represented, suggesting that certain species are highly susceptible to NDV infection and likely to be reservoirs [14]. Spillover of class I NDV from wild birds to poultry does occur and these avirulent viruses have the potential to become virulent over time by: i) gaining basic amino acids near the F protein cleavage site; ii) transmission from large mobile populations of wild birds; and iii) escape of live vaccine strains from poultry farms into the wild bird environment [14]. Although the most likely reservoir of velogenic NDV is the vaccinated poultry population there is evidence that wild birds may represent natural reservoirs of mesogenic viruses, some of which are used as vaccine strains [1].

Low virulence class I and mesogenic viruses of class II and genotypes V or VI predominate in cormorants and pigeons. In contrast the viscerotropic velogenic NDV are predominant in vaccinated poultry, suggesting that the immune pressure from vaccination may be selecting variant forms of velogenic NDV. The persistence of velogenic NDV in poultry despite intensive vaccination efforts has been a recurrent phenomenon in endemic countries of Asia, Africa and Central America [14]. Genetic homogeneity (intensive poultry production), high-density rearing (increasing the number of “effective contacts”), and intensive vaccination programs may be contributing to the evolution of virulent NDV [14]. Epidemiological and value chain links at the interface between smallholders, intensive poultry production and wild birds should be considered prior to embarking on a vaccination program.

Environmental Factors

Following removal of organic matter, NDV is susceptible to 1% phenol or quaternary ammonium disinfectants; ultraviolet light, acidic hydrogen based chemical agents (e.g. Virkon). NDVes can survive for several weeks in the environment, especially in cool weather.

A meta-analysis of epidemiological studies conducted in Africa between 1980 and 2009 has identified environmental (Figure 5) and seasonal correlations with the occurrence of NDV. The study found country specific patterns for outbreaks with corresponding vaccination schedules (Figure 6) [15].



Incubation period (domestic chicken) (f)	Ordinary 4–6 d	Minimum 2–6 d	Maximum 15–21 d
Mode of transmission (g)	Faecal–oral ++	Respiratory +	
pH (f)	3–11 Survival 1 week		
Inactivation temperature (a–f)	(°C) 60 °C 56 °C	Time (h) 0.5 h 3 h	

Figure 5: Meta-analysis of NDV survival characteristics from studies conducted in Africa, 1980-2009

In general, NDV is most common encountered during dry winter months in Southeast Asia, and generally also the dry season in African countries (Figure 6) [15].

Exposure and seroconversion is greater in backyard village than commercially raised poultry, likely due to housing and accessibility of wild birds [15]. Human movement, cultural practices, marketing and poultry

vaccinators are also important risk factors for transmission and spread of NDV [15]. Value chains play an important environmental risk for exposure. Studies in Mali, Ethiopia and Madagascar highlight the importance of trade and attendance at a market and the vicinity of traders are correlated to a higher prevalence of NDV virus on farms [12][13][16]. In Madagascar, the risk of infection at the district level is statistically related to the density of trade flows. Similarly, the risk of virus circulation increases in markets because of the high density of domestic birds coming from different areas [17].

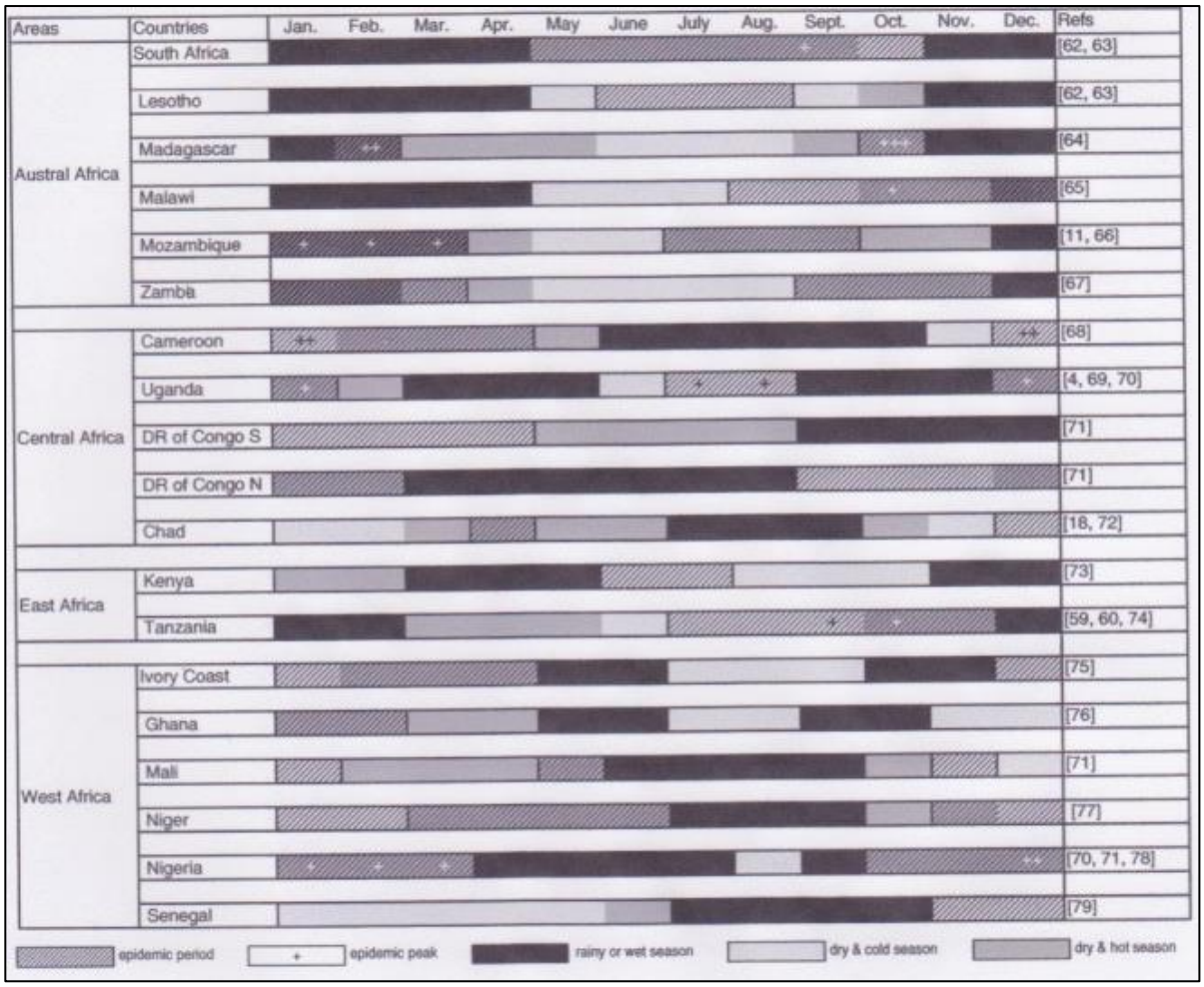


Figure 6: Meta Meta-analysis of NDV seasonality related to outbreaks and vaccination from studies conducted in Africa, 1980-2009

Clinical Signs

Clinical signs vary depending on: virus virulence; dose; route of transmission (respiratory is fastest); host species; breed; age; host immune status (exposure and vaccination history); and other factors. The official incubation period for OIE is 21 days however the biological incubation period is between 2-15 days, with most cases occurring within 5-6 days following exposure but possibly as long as 3-4 weeks. Species susceptibility in decreasing order to NDV is as follows: chickens, turkeys, pheasants, pigeons and ducks. The main clinical signs are as follows [1]:

1. Viscerotropic velogenic NDV
    a. Unvaccinated chickens: Listlessness, severe lethargy and 100% mortality within 3-4 days; following ocular nasal transmission: bilateral conjunctivitis, severe swelling of eyes, combs, wattles, clear mucus exuding from the mouth, drooping head and green watery diarrhea;
    b. Vaccinated chickens: drop in egg production with misshapen or bleached eggs one month after infection.

2. Neurotropic velogenic NDV
    a. Unvaccinated chickens: Excitability during the first 3-4 days followed by tremors, torticollis, and paralysis of one wing or leg and failure to access feed and water with death after 9 days; 50% mortality in older birds but higher in young birds;
    b. Chicken isolates can cause neurological signs in pigeons.

3. Mesogenic NDV strains in unvaccinated chickens: tremors, torticollis, and paralysis but limited mortality; pigeon isolates may lead to asymptomatic infections.

4. Lentogenic NDV: no clinical signs in adults, but naïve unvaccinated birds or birds vaccinated with live La Sota strain can show respiratory signs: mild to serious respiratory distress. Note: Poor vaccination technique can result in incomplete vaccination of flocks and a "rolling reaction" whereby replication, amplification and host adaptation Increasing virulence) of live virus results.

Diagnosis

"The severity of disease produced varies with both host and strain of virus. Even APMV-1 strains of low virulence may induce severe respiratory disease when exacerbated by the presence of other organisms or by adverse environmental conditions (ammonia). The preferred method of diagnosis is virus isolation and subsequent characterization" [2]. NDV is immunosuppressive and increases susceptibility to other viruses, bacteria and parasites [1].

Differential Diagnosis

The symptoms and pathology of NDV are not pathognomonic and the main differential diagnoses of NDV include LPAI and HPAI pathotypes, as well as aspergillosis, mycoplasmosis, ILT and IB [1].

Gross pathology

Lesions seen in birds will depend on their previous exposure to wild virus or to NDV vaccine. In non-vaccinated or exposed birds the following gross lesions can be observed and the main clinical and pathological observations are summarized in Table 3 [1][2].

Table 3: Main clinical and pathological features of viscerotropic velogenic (VV), neurotropic velogenic (NV), mesogenic (M), lentogenic (L) and asymptomatic (A) pathotypes in chickens.

Clinical/Pathological Hallmarks	VV	NV	M	L	A
Hemorrhagic necrosis of diffuse lymphoid tissues of the intestine	+++	+/-	-	-	-
Enlarged spleen	+++	-	-	-	-
Hemorrhagic necrosis of laryngeal tonsils and upper trachea	+++	-	-	-	-
Swelling of head, face, eyes	+++	-	-	-	-
Hemorrhagic necrosis of comb, wattles and face	+++	-	-	-	-
Egg yolk peritonitis	+++	-	-	-	-
Mortality	+++	+++	++/+	+	-
Respiratory difficulty	+++	+++	++	+	-
Depression	+++	+++	++	+/-	-
Optisthotonus		+++	+/-	-	-
Torticollis		+++	+/-	-	-
Enteritis	+++	-	-	-	-
No clinical/pathological signs	-	-	-	+/-	+++

Legend: Severe/High (+++); Moderate (++); Mild (=); None (-)

Diagnostic Tests

OIE Terrestrial Manual Chapter 2.3.14 outlines the following diagnostic tests for NDV [2]: Samples should be collected from recently dead birds or moribund birds that have been killed humanely. Identification of the agent is done as follows:

- Dead birds: oro-nasal swabs; lung, kidneys, intestine (including contents), caecal tonsils, spleen, brain, liver and heart tissues, separately or as a pool;
- Live birds: tracheal or oropharyngeal and cloacael swabs (visibly coated with faecal material) from live birds or from pools of organs and faeces from dead birds;
- Special attention should be given to appropriate types of media for shipping

Identification of NDV

1. VI from inoculation of embryonated eggs. Samples from live birds should include both tracheal or oropharyngeal and cloacal swabs (collected and stored separately), the latter should be visibly coated with fecal material. Swabbing may harm small, delicate birds, but the collection of fresh feces may serve as an adequate alternative.
2. HA activity detected from inoculated eggs may be due to the presence of any of the ten subtypes of APMV (including NDV) or 16 hemagglutinin subtypes of influenza A viruses, or. Nonsterile fluid could contain bacterial HA. NDV can be confirmed by the use of specific antiserum in a hemagglutination inhibition (HI) test. Usually chicken antiserum that has been prepared against one of the strains of NDV.
3. ICPI: Fresh infective allantoic fluid with a HA titre $>2^4$ (>1/16) is diluted 1/10 in sterile isotonic saline with no additives, such as antibiotics. 0.05 ml of the diluted virus is injected intracerebrally into each of ten chicks hatched from eggs from an SPF flock. These chicks must be over 24-hours and under 40-hours old at the time of inoculation. ICPI is the mean score per bird per observation over the 8-day period.
4. Molecular method: requirement of at least one pair of basic amino acids at residues 116 and 115 plus a phenylalanine at residue 117 and a basic amino acid (R) at 113 if the virus is to show virulence for chickens. Failure to detect virus or detection of NDV without multiple basic amino acids at the F0 cleavage site using molecular techniques does not confirm the absence of virulent virus and the ICPI must be performed.
5. Monoclonal antibody panels have been developed.
6. Phylogenetic studies [8].
7. RT-PCR with appropriate primers.

Serological tests

1. HA and HI tests
2. ELISA kits are available and based on several different strategies for the detection of NDV antibodies, including indirect, sandwich and blocking or competitive ELISAs using MAbs. At least one kit uses a subunit antigen. Conventional ELISAs have the disadvantage that it is necessary to validate the test for each species of bird for which they are used. Competitive ELISAs may not recognize all strains of APMV-1 if they use Monoclonal Antibodies known for their specificity for single epitopes.

Although all APMV-1 viruses are of the same serotype, minor variations can be detected by using the VN test [1]. Many Asian countries (including India and Pakistan), rely of mesogenic strains to induce protective immunity in vaccinates to more virulent forms [1]. Ideally a useful vaccine will permit the ability to DIVA, particularly when the disease is rare. This can be accomplished by designing a vaccine with a marker found in heterologous or subunit vaccines. DIVA strategies for NDV have not yet been developed.

Zoonotic disease

NDV is a zoonotic disease, which may result in mild conjunctivitis in humans. Laboratory personnel, poultry owners, farm workers, and veterinarians who handle poultry are at highest risk. Transmission can occur via infected oral, ocular and cloacal contents or via aerosol [1]. Immunosuppressed individuals are particularly vulnerable, however no person-to-person spread has been reported.

Incidence and Prevalence in Selected Countries

Global

Although Newcastle disease is one of the most important diseases impacting the health of poultry and the health and livelihoods of the rural poor, it remains grossly under-reported globally [3][17]. It is estimated to be the 7th leading cause of animal losses globally as expressed by livestock units presented in Tables 4 [21].

Table 4: Ten leading disease losses globally by livestock disease units (LSU) loss

Diseases by LSUs Lost — Number of LSU Lost						
		Average 2006–2009				Change 2009 vs. average 2006–2008
Rank	Disease	by death	by destruction	by slaughter	Total	
1	HPAI	11,202	85,517	2	96,721	-83%
2	Echinococcosis	24	5,837	84,130	89,991	-9%
3	Avian infectious bronchitis	83,992	164	112	84,268	196%
4	Bovine tuberculosis	486	15,998	56,532	73,015	30%
5	Low-pathogenic avian influenza	60,260	9,966	457	70,683	128%
6	Enzootic bovine leukosis	121	61,148	6,912	68,181	-6%
7	Newcastle disease	35,980	23,795	595	60,370	9%
8	Brucella abortus	455	15,277	17,176	32,908	29%
9	Infectious bursal disease	26,644	239	202	27,085	118%
10	Classical swine fever	6,361	12,741	2,851	21,953	-57%

Table 5: World Bank definition of livestock units (LSU)

1 camel or "other camelid"	=	1.1 LSU
1 cattle	=	0.9 LSU
1 buffalo	=	0.9 LSU
1 horse or mule (equidae)	=	0.8 LSU
1 pig	=	0.25 LSU
1 sheep	=	0.1 LSU
1 goat	=	0.1 LSU
1 poultry bird (chicken, duck, guinea fowl or goose).	=	0.015 LSU

Regional

From a total of 21,370 NDV events reported in the 20 selected countries considered under the LVIF between 2000 and 2015, about 5,290 (25%) NDV disease events were reported from 14 selected African countries and 16,080 (75%) NDV disease events were reported from 6 selected Asian countries. Reporting bias must be considered when interpreting these estimates. Mesogenic and velogenic NDV pathotypes occur in all Asian countries. In 2014-2015, India recorded 311 outbreaks of NDV (Ranikhet) based mainly on passive surveillance [22]. A regional map of NDV reported for Africa in 2011 is presented in Figure 7 and NDV is reported the most commonly animal disease among all African countries [16]. The four countries with the highest number of reported ND outbreaks in Africa include Zambia (n=137), Ghana (n=127), South Africa (n=86) and Botswana (n=82).

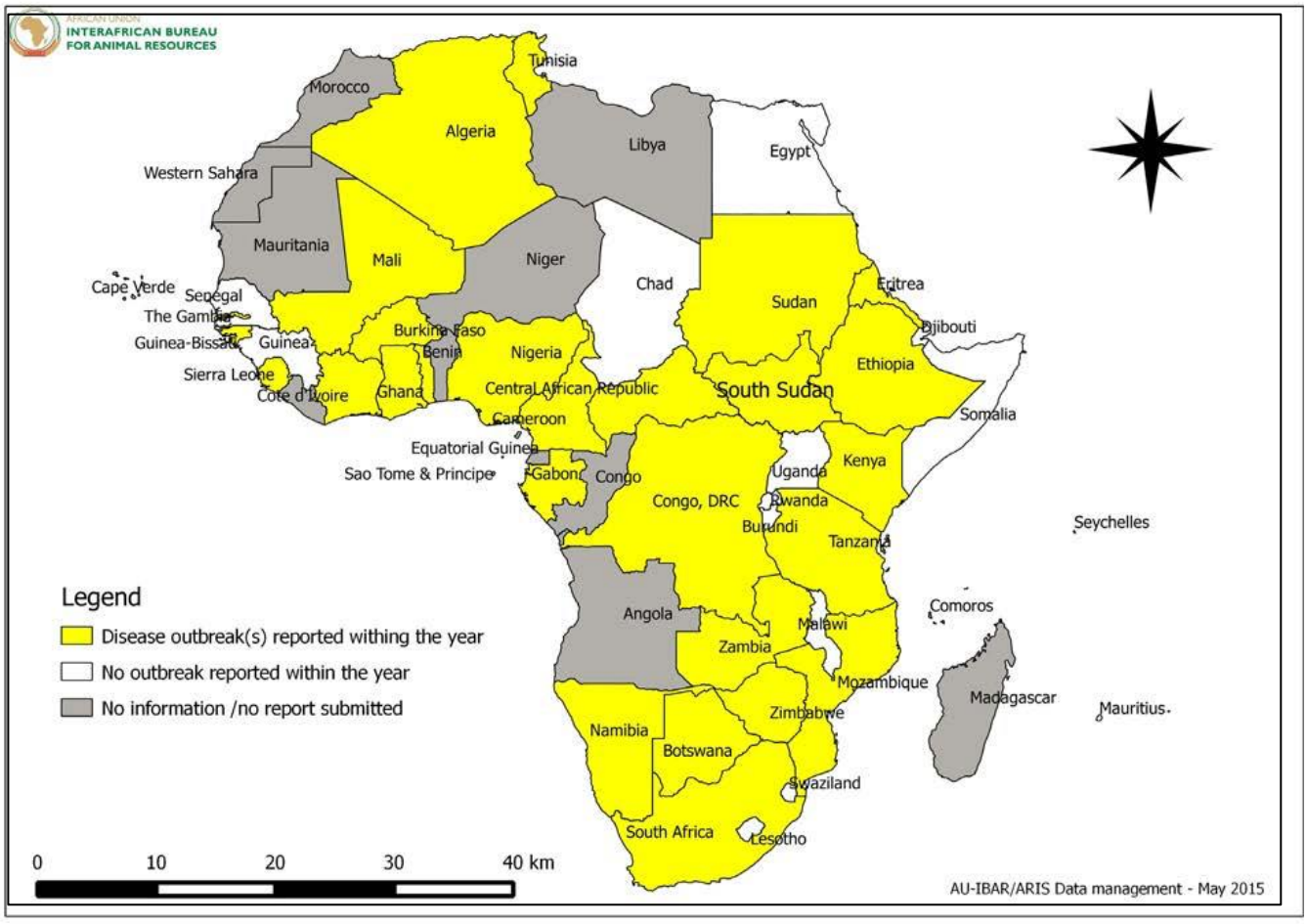


Figure 7: Spatial distribution of NDV events reported in Africa during 2011.

Tables 6 and 7 summarize the estimates of incidence and prevalence from NDV events reported and studies conducted, respectively in the 20 selected countries between 2000 and 2015. In Africa, the prevalence of NDV in wild birds and poultry is estimated to be 3% and 67% respectively [15][18].

Table 6: Incidence of Newcastle disease outbreaks in 20 selected countries, 2000-2015.

Region/Country	Reported Incidence NDV (OIE, WAHID) http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/statusdetail# (Accessed 20 October 2015)														
	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**
Sub Saharan Africa															
Burkina Faso	6	11	4	2	8	11	10	54	25	75	126	66	27	15	60
Ethiopia	8	34	67	16	40	70	84	28	29	35	84	68	40+	150	50
Ivory Coast	…	…	…	…	…	?+	0	…+	3	8	19+	7	8	8	6
Kenya	5	11	10	2	3	1+()	63	6	1	?	19+	2+	7	2	9
Madagascar	55	…	83	47	24	13	16	4+	…+	…+	10	4	5	14	8
Malawi	36	…	12	6	…	1	1+	2	…+	…+	2	3	10	5	…
Mali	1	0	0	0	0	…+	3	?	2?	14	8	4	0	1	1
Mozambique	3	9	6	7	15	12	5	4	5	2+	4	2+	6	4	3
Rwanda	…	…	…	…	0	…	36	13	68+	30?	…+	…	…+	17	…
Senegal	2	1	17	4	2	1	4	4	1	3	2	2	…+	2	2+
South Africa	9	4	2	4	4	175	126	66	64	17	27	22	25	47	97
Tanzania	40	49	126	147	57	91	44	129	34	25	25	17	14	10	10
Uganda	58	110	103	86	53	9	1+	…+	…+	…+	…+	…+	…	…+	…+

Zambia	36	17	63	43	60	…	40	79	136	162	152	…+	68	177	171
South Asia															
Bangladesh	…+	…+	…+	…+	…+	…+	…+	…+	…+	…+	…+	…+	…+	…+	…
India	464	633	812	338	323	391	391	280	230	389	497	886	645	423	311
Nepal	261	211	190	135	48	147	87	46	16+	128	210	275	312	132	92
Southeast Asia															
Indonesia	…	…	…	…	…	…+	…+	…+	…+	…+	…+	…+	…+	…+	…
Myanmar	74	151	119	64	87	…+	43	75	29	35	14	7	14	10	7
Vietnam	134	…	…	47	…	114	807	1174	1156	928	1181	180	94	77	70

WAHIS Codes 2005-2015

[**...** - No information available for this disease; **0** - Disease absent; **?** - Disease suspected; **? +** - Infection/infestation; **...+** - Disease present but without quantitative data; **+** - Disease present with quantitative data but with an unknown number of outbreaks; **+()** - Disease limited to one or more zones]

HandiStatus II Codes 2000-2004:

[**0** - Disease never reported; **?** - Disease suspected but presence not confirmed; **…+** - Reported present or known to be present; **…** - No information available]

Table 7: Prevalence estimates of NDV in 20 selected countries.

Region/Country	Apparent Prevalence (95% CI)	Study Design	Time Period	Reference
Sub Saharan Africa				
Burkina Faso	13.8% (39/283) samples positive	Active surveillance in outbreak areas	2006	Tamagda et al, 2011
Ethiopia	0.70%	Cross-sectional serosurvey	2011-2012	Betteridge, 2014
	30.1% virus positive	Cross sectional live bird market survey	2012	Mulisa et al, 2014
Ivory Coast	19.80%	Active prospective backyard serosurvey	2007-2009	Couacy-Hymann, 2012a
	0.3-1.4%	Active, prospective, live market and backyard flock virus surveillance	2009-2010	Couacy-Hymann, 2012b
	22% seropositive; 14.7% virus positive	Active, prospective, live market and backyard flock virus surveillance	2010-2012	Kouaku, 2015
	Virus prevalence of 15% in 2006 to 2008 compared to prevalence of 0.3 to 1.4% in 2010	In Ivory Coast, only sick birds were sampled	2006-2011	Snoeck et al, 2013
Kenya	NDV higher (17.8%) in the dry hot zone (lower midland 5) compared to the cool wet zone (lower highland 1) at 9.9%	Free range chicken farms	NA	Njagi, et al, 2010
Madagascar	Seroprevalence of 60% (non-vaccinated animals, (CI 95 57–63%), n = 778)	Cross-sectional serological study	2008	Andriamanivo et al, 2012

Region/Country	Apparent Prevalence (95% CI)	Study Design	Time Period	Reference
Malawi				
Mali	ND seroprevalence was 58.4%, and the odds of seropositivity was 2.0 higher in chickens than in ducks, 1.7 higher in females than in males, 3.1 higher in adults than in young birds; NDV virus prevalence of 2.6%	Prospective serosurvey among 1470	2007-2008	Molia et al, 2011
Mozambique	66 percent of households who raised chickens had losses due to NDV	TIA National Agricultural Survey	2005-2006	Tomo, 2009
Rwanda				
Senegal	Seroprevalence was 54.4% in rural chickens	Prospective serosurvey of rural poultry	2008	Kone et al, 2013
South Africa				
Tanzania	The highest seroprevalence (81.5) and virus isolation frequency (18/27) were found in the period between June and October	Retrospective data and prospective cross sectional study	Since 1994	Yongolo, 1996
Uganda	80.4% of households had lost chickens	Baseline KAP study	2003	Mbabazi, 2012
Zambia	Seroprevalence of NDV) in chickens in Zambia was 36.9% based on HI titres of 2000 blood samples	Seroprevalence based on 2000 samples	NA	Alders et al, 1994
South Asia				
Bangladesh	7.5% of 1653 dead or sick bird laboratory submissions	Retrospective secondary data analysis	1999-2000	Giasuddin et al, 2002

Region/Country	Apparent Prevalence (95% CI)	Study Design	Time Period	Reference
India				
Nepal				
Southeast Asia				
Indonesia				
Myanmar	Median month-specific, village-specific mortality rates per 1000 bird-days at risk (counting missing birds as deaths) ranged from 0.8 to 1.7 for adults, from 0.4 to 4.7 for growers and from 8.0 to 16.5 for chicks	Longitudinal study to describe temporal patterns of mortality of village chickens in 10 villages in Myanmar.	2003-2004	Henning et al, 2008
Vietnam	Seroprevalence of NDV- antibody titers (> log2 3) was 47.7% (n = 81)	Prospective serosurvey	NA	Vui et al, 2002

Conclusions from incidence and prevalence data

It can be assumed that country reports are largely representing velogenic and mesogenic pathotypes. This assumption is supported by data from Bangladesh where a 7.5% prevalence estimate was obtained from laboratory data that is gathered passively from voluntary submissions, despite no official incidence reporting to the OIE. Another confounding issue is that viruses are rarely pathotyped, further affecting the accuracy of the estimates, since lentogenic NDV are ubiquitous and very common due to natural incidence or escape of live lentogenic vaccine strains used (e.g. La Sota). NDV is a disease, which poultry owners expect and accommodate to each year and therefore underreporting is generally accepted in both Asia and Africa. In terms of reported incidence Figure 8 depicts the ordered number of reports received, which reflect both incidence and reporting intensity. Incidence data from the OIE is useful to show relative trends in reporting and qualitative estimates among the selected countries (Figure 8).

Prevalence data reflect the methodologies used. LBM surveys are economical and easy to conduct as an initial scanning, targeted surveillance. Household surveys are useful but costly to conduct however they give an accurate local estimate for a vaccination program and are more reliable to assess the initial risk as well as the impact of both NDV itself and a vaccination program. Development and implementation of a vaccination program including community outreach should consider these reporting biases.

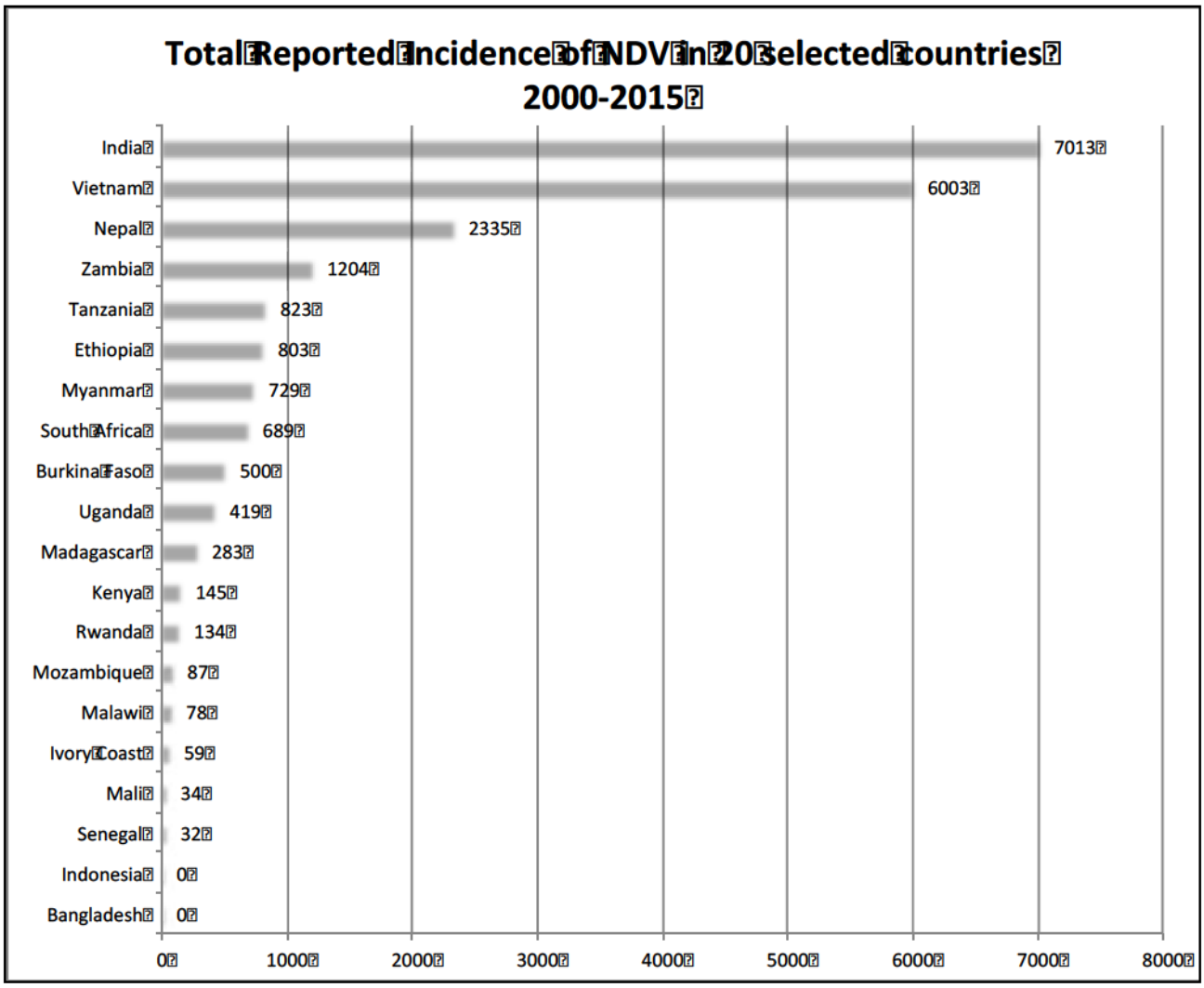


Figure 8: Total Reported Incidence of NDV in 20 selected countries 2000-2015.

Economic and Social Impacts at Global and Regional Levels, and in Selected Countries

Figure 9 summarizes the relationship between farmer income (log scale) and exposure risk (impact probability) to NDV at the regional level [19]. South Asia, sub-Saharan Africa and Southeast Asia rank as the top three most impacted regions globally. This figure suggests that Newcastle disease is endemic in South Asia and sub-Saharan Africa, where smallholder poultry represents nearly 80% of the total poultry holders, while recurrent epidemics occur in regions with a mix of intensive and extensive poultry production. The intensive poultry producers of Australasia and North America maintained Newcastle disease-free status, as did the Island States of Oceania. Underreporting played a role, as was most likely the case for Central Asia [20]. Poultry provide animal protein in the form of meat and eggs and can be sold or bartered to meet essential family needs. Village poultry are active in pest control, provide manure, are required for special festivals and are essential for many traditional ceremonies. They are generally owned and managed by women and children and are often essential elements of female-headed households [20]. The economic impact of Newcastle disease among selected countries in terms of lost livestock units between 2006-2009 was greatest in South Asia and Viet Nam as demonstrated in Figure 10 [21].

The costs of NDV epidemics include lost production, lost trade and disease control [23]. In Bangladesh, a successful production model has been developed which involved more than 2 million women (households). This model has a structured approach to improve smallholder poultry production and health, and socio-economic development at village level **Error! Reference source not found.**]. For smallholder vaccine programs to be s uccessful and sustainable, communities must take responsibility and be empowered to develop and implement solutions that meet the local needs. Similarly, there is a need to initiate a major shift away from the traditional production-based research to a new approach that is market-driven, focused on trade and poverty alleviation. This shift must include a more effective linkage with the private sector and their resources and skills [25].

For such an important disease affecting rural households globally, relatively little quantitative microeconomic information is available specific to Newcastle disease. Studies estimating the qualitative social and economic impact of Newcastle disease related to the 20 selected countries are summarized below in Table 8.

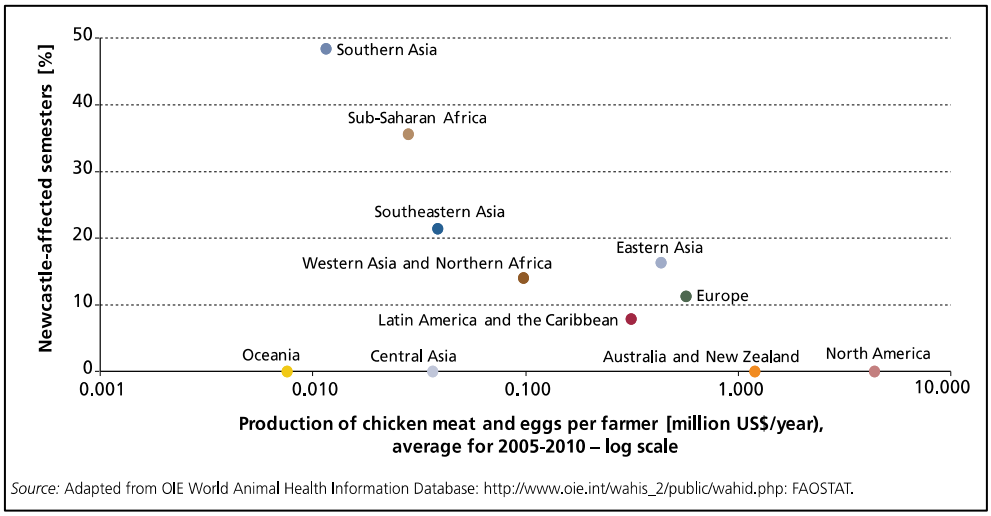


Figure 9: Relationship between farmer income (log scale) and exposure risk (impact probability) to NDV at the regional level [20]

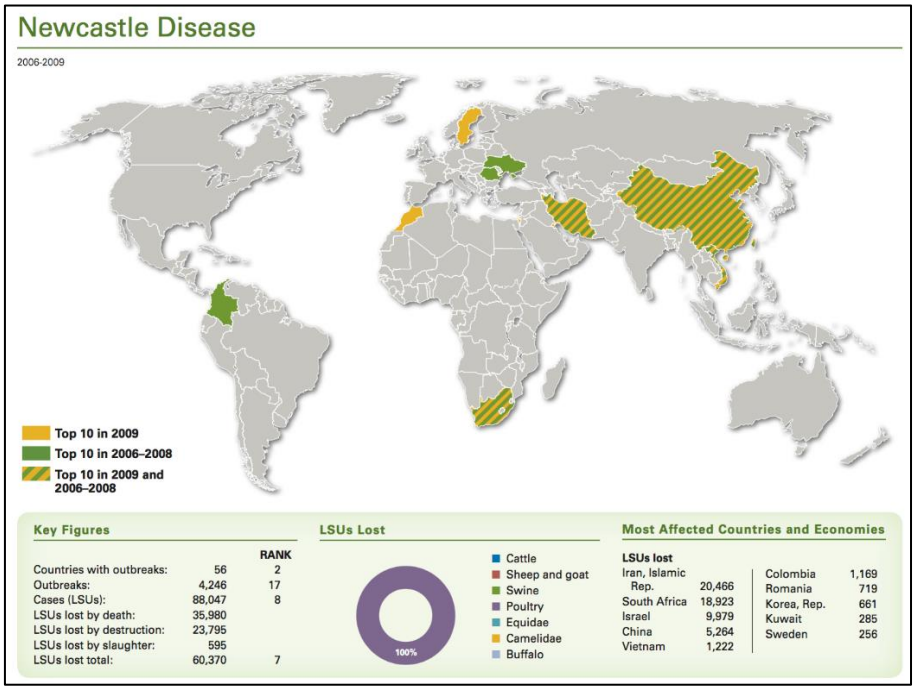


Figure 10: Relationship between farmer income (log scale) and exposure risk (impact probability) to NDV at the regional level [21]

Table 8**: Socioeconomic impact of Newcastle disease in 20 selected countries**

Region/Country	Economic Impact	Social Impact	Reference
Sub Saharan Africa			
Burkina Faso	A survey achieved in 1998 in the project area revealed that the mortality rate were between 13-90% for chickens. No economic data given.		Minoungou, 2009
Ethiopia			
Ivory Coast			
Kenya			
Madagascar			
Malawi			
Mali			
Mozambique	In the south of Mozambique, women have been able to sell excess chickens in order to buy goats and eventually cattle	Decreased chicken numbers, increased household purchasing power, increased home consumption of chicken products and increased decision-making power for women	Alders and Pym, 2009
	Decreased access to cash or goods through exchange, but it also represents the possibility of gaining access to a good meal of higher nutritional value, and improved		Bagnol, 2001

	food security; 50 to 100 percent of deaths annually in rural households		
Rwanda			
Senegal			
South Africa			
Tanzania		Increased chicken numbers, increased household purchasing power, increased home consumption of chicken products and increased decision-making power for women	Alders and Pym, 2009
	Of the approximately 30 million chickens kept in Tanzania, 28 million are free-range village chickens [1]. They provide livelihood and supply 100% of eggs and chicken meat consumed in rural areas, where 83% of the population lives. In addition, they cater for 20% of the chicken egg and meat demand of urban consumers [2]. Free-range chickens have an important role in economic and nutritional needs of the Tanzanian people.		Yongolo et al, 1996
Uganda			
Zambia			

South Asia		Impact studies have demonstrated that income from the sale of eggs in South Asia is used to educate children.	Alders, 2009
Bangladesh	30% annual poultry losses at household level due to NDV		Giasuddin et al, 2002
India			
Nepal			
Southeast Asia			
Indonesia			
Myanmar			
Vietnam	Qualitative assessment: Newcastle disease is the most important cause of mortality in chickens		Vui, 2002

Disease Prevention and Control Methods

Treatment (Control)

Medical Treatment

There is no medical treatment for NDV in poultry. Sanitary control measures are similar to those for AI including the following:

Sanitary Control Methods

Table 9 summarizes control measures recommended by the OIE (left column) with feasibility assessments in smallholder poultry settings [3].

Table 9: Feasibility of OIE recommended sanitary control measures in smallholder poultry settings.

Sanitary Control Measures	Feasibility in Smallholder Setting
Movement Controls	Limited: due to continual mixing and marketing of poultry
Aggressive active surveillance	Variable depending on technical capacity and cooperation
Biosecurity measures	Limited: isolate, clean and disinfect, dispose of carcasses
Culling	Limited: human habit of eating sick and dead poultry and rarely a policy option in developing countries unless trade is important
Vaccination	Possible during an outbreak but not advised (see next point)
Training	Vaccinators and animal health officials can spread disease
Risk communication	High if village leaders are engaged

Prophylaxis (Prevention)

Sanitary Prophylaxis

Table 10 summarizes measures are recommended by the OIE (left column) with feasibility assessments in smallholder poultry settings [3].

Table 10: Feasibility of OIE recommended sanitary prevention measures in smallholder poultry settings

Sanitary Prevention Measures	Feasibility in Smallholder Setting
Bird-proofing houses, feed and water supplies	Limited: for feral poultry; Moderate for confined village poultry
Proper carcass disposal	Variable depending on food security needs
Pest control in flocks; insects and mice	Limited: to confined village poultry
Avoidance of contact with birds of unknown health status	Limited: constant animal and human movement driven by an economic incentive
Control of human traffic	Limited: (see above)
Control of vehicular traffic	Limited: (see above)
Quarantines and movement controls	Limited: (see above)
Thorough cleaning and disinfection of the premises 21 days before restocking	Limited: contaminated ground cannot be sterilized; Moderate for confined village poultry

In conclusion, sanitary prevention and control options are very limited, prophylactic vaccination is the most realistic option for long-term prevention and control of NDV. Source reduction is possible with vaccination by reducing the amount of circulating virus in the population and in the environment. Elimination is not possible since NDV of different pathotypes remain endemic throughout the inhabited world, including the developed world where lentogenic strains persist and vaccination is still relied upon to manage the disease.

Medical Prophylaxis

Given the challenges of sanitary measure discussed above, medical prophylaxis using vaccination will permit pathogen reduction and control. Below are typical NDV vaccination program schedules using traditional live attenuated and inactivated oil emulsion vaccines that are tailored to control the circulating challenge field genotype and pathotype.

NDV strains used in conventional commercial live virus vaccines fall into two groups [3][27]:

- Lentogenic vaccines, such as Hitchner-B1, La Sota, V4, NDW, I-2, F – Priming dose (or booster dose)
- Mesogenic vaccines, such as Roakin, Mukteswar and Komarov – Prime or booster dose.

Vaccine master seed virus strains should not have an intracerebral pathogenicity index ICPI exceeding 0.4. Examples of vaccine use in low risk and high situations are depicted in Figure 11 [2].

Example protocol when NDV field pathotype is mild or sporadic:

- Live La Sota by conjunctival (eye drop) or spray administration at 1 day of age;
- Live Hitchner-B1 or La Sota at 18–21 days of age in the drinking water;
- Live La Sota in the drinking water at 10 weeks of age; and
- Inactivated oil emulsion vaccine at point of lay.

Example protocol when NDV field pathotype is severe or endemic:

- Live La Sota by conjunctival or spray administration at 1 day of age;
- Live Hitchner-B1 or La Sota at 18–21 days of age in the drinking water;
- Revaccination at 35–42 days of age with live La Sota in the drinking water or as an aerosol;
- Repeat at 10 weeks of age with an inactivated vaccine (or a mesogenic live vaccine); and
- Repeat at point of lay.

Strain	Description
F	Lentogenic. Usually used in young chickens but suitable for use as a vaccine in chickens of all ages.
B1	Lentogenic. Slightly more virulent than F, used as a vaccine in chickens of all ages.
La Sota	Lentogenic. Often causes post vaccination respiratory signs, used as a booster vaccine in flocks vaccinated with F or B1.
V4	Avirulent. Used in chickens of all ages.
V4-HR	Avirulent. Heat Resistant V4, thermostable, used in chickens of all ages.
I-2	Avirulent. Thermostable, used in chickens of all ages.
Mukteswar	Mesogenic. An invasive strain, used as a booster vaccine. Can cause adverse reactions (respiratory distress, loss of weight or drop in egg production and even death) if used in partially immune chickens. Usually administered by injection.
Komarov	Mesogenic. Less pathogenic than Mukteswar, used as booster vaccine. Usually administered by injection.

Figure 11: Summary of the live NDV vaccine strains [26]

The level of (blocking) maternal antibodies is important to consider when vaccinating progeny. Route of administration and adjuvant are also very important to achieve both the level of safety and efficacy needed to protect the flock from field challenge. Post-vaccination seromonitoring using the ELISA or HI test is always advised and periodic challenge tests may be required to make adjustments to the prevailing genotype. Live attenuated vaccines have the potential to increase in pathogenicity when incomplete flock immunity occurs due to inadequate vaccination technique [1][2].

Options and Strategies for Vaccination

A realistic objective for a sustainable smallholder poultry vaccination program is to control (manage) NDV rather than attempt to eliminate the virus since: 1) Lentogenic NDV are ubiquitous; 2) Mesogenic NDV are endemic in many African and Asian countries; 3) biosecurity options are limited; and 4) vaccination achieves reduction in shedding but does not produce sterilizing immunity [1][2][3][26]. Categories of NDV vaccines available, their advantages and example are summarized in Table 11.

Alders and Pym offer five recommendations for sustainable NDV vaccination programs poultry smallholders [20].

- An appropriate vaccine, vaccine technology and vaccine distribution mechanisms;
- Effective extension materials and methodologies that target veterinary and extension staff as well as community vaccinators and farmers;
- Simple evaluation and monitoring systems of both technical and socio-economic indicators;
- Economic sustainability based on the commercialization of the vaccine and vaccination services and the marketing of surplus chickens and eggs, and
- Support and coordination by relevant government agencies for the promotion of vaccination programs.

Important strategic considerations for selecting an appropriate NDV vaccine are summarized below:

1. Simple to apply in communities based on needs and capacities of the communities and the technical resources of the government.

2. Fit for purpose – Monovalent vaccines are more cost effective and targeted for specific needs to control NDV for smallholder populations. However, in some situations bivalent or multivalent choices may be needed to control other diseases, depending on cost. Vaccine administered via eye drop is more likely to result in owner compliance since it is simple to perform, non-invasive and is does not cause adverse tissue reactions [20][27].

3. Epidemiologically appropriate – Possible reversion of live lentogenic or mesogenic strains used to vaccinate commercial poultry should be considered when planning a smallholder vaccination program [1][20].

4. Ability to license vaccine – Some countries such as Indonesia does not permit the use of genetically modified recombinant vaccines [28].

5. Antigenically appropriate – Seromonitoring and challenge studies inform vaccine choice based on genotype [1][14].

6. Thermostability – I-2 vaccine and other similar vaccines allow flexibility to increase the efficiency and uniformity of poultry immunization [27].

7. Broad age-based application in multi-age flocks typical of village smallholder flocks [27].

8. Use of multivalent vaccines may be a scientifically valid approach to take when it is possible. The reality in the field is that many economically significant poultry diseases are neither reported nor assessed quantitatively, particularly NDV. Vaccine cost as well as farmer and government perception of risk must be carefully assessed in order to prioritize resources for sustainable, self-directed vaccination programs. Needs assessments of the primary stakeholders should first be conducted prior to embarking on prevention and control through vaccination. In this way, vaccination, biosecurity training and surveillance systems incorporated specific measures for priority diseases as well as NDV. The use of NDV-AI vaccines can be considered depending on the results of an epidemiological risk assessment.

I-2 is the first Thermostable NDV vaccine developed and is well suited for use with smallholder poultry populations [29][30]. Important characteristics favouring its use follow:

- Thermostable for 8 weeks at 28°C when in freeze-dried form and stored in the dark;
- A minimum of 106 EID^{50}/bird is required to produce adequate protection;

- Can be administered via eye drop, drinking water, certain feeds and injection
- Eye drop administration of the vaccine produced a greater survival rate, had a lower frequency of administration and was easy;
- Confirm that the eye-dropper to be used is made of virus- friendly plastic and that it be calibrated to ensure that one drop contains one dose;
- The same dose is given to birds of all ages, from day 1 to adults
- I-2 ND vaccine spreads from vaccinated to unvaccinated birds when housed together
- Safe to both bird and handler. It produces no evidence of clinical respiratory signs, weight loss, mortality in young chickens or egg production drop
- 80% protection in the field in the face of an outbreak, when given every 4 months via eye drop.
- Cost per dose in 2001 was USD 0.005 (In 2015 in Tanzania, cost is USD 0.01, personal communication, D. Suarez)

Table 11: Government Policies and Public/Private Domains for 20 selected Countries

Newcastle Disease (ND)	Notifiable	Official surveillance[1] program	Official control [2] program	Vaccination				Treatment/Chemotherapy	
	(yes/no)	(yes/no)	(yes/no)						
Country				Compulsory vaccination	Who pays for the vaccine?	Who delivers the vaccine?	Species vaccinated	Treatment authorised	Frequently practiced
				(yes/no)	(Government, farmers, combination, others- specify)	(official, private vaccinators or both)	(cattle, sheep, goats, pigs, poultry)	(yes/no)	(yes/no)
Burkina Faso									
Ethiopia									
Ivory Coast	OUI	PASSIF MAIS ACTIF EN CAS D'EPIZOOTIE	OUI	OUI	GOUVERNEMENT ELEVEUR ORGANISMES	GOUVERNEMENT	VOLAILLES	NON	
Kenya	yes	Yes, passive	no	no	farmers	both	poultry	yes	yes
Madagascar									
Malawi	YES	YES (PASSIVE/ACTIVE)	YES	YES	COMBINATION	BOTH OFFICIAL AND PRIVATE	POULTRY	N/A	N/A

Mali	Yes	Yes, passive	Yes	Yes	COMBINATION	Both	poultry	No	No
Mozambique									
Rwanda	Yes	Both	Yes	Yes	Farmers	Official	Poultry	No	No
Senegal									
South Africa									
Tanzania	yes	Yes, passive/active	Yes, in the process	yes	Government/ private, Ngo	both	Poultry	no	no
Uganda	YES	NO	NO	NO	FARMERS	PRIVATE	POULTRY	YES (SECONDARY)	YES
Zambia	Yes	Yes - passive	Yes	Yes	Combination	Both	Poultry	No	No
Bangladesh	Yes	Yes (Passive)	Partial	No	Combination (1) Govt Vaccine: Govt.: Subsidy, Owner pays service charge)(2) Private Vaccine: Owner	Government and Private	Poultry	No	Yes
India									
Nepal	No	yes/passive	No	No	combination	both	poultry	N/A	N/A
Indonesia									

Myanmar	yes	yes(passive)	no	no	Government, Farmers	Both	poultry	no	yes
Vietnam	Yes	Yes/Passive	No	Yes	Farmers	Both	Poultry	No	Yes

[1]Surveillance: is the systematic on-going collection, collation and analysis of data and the timely dissemination of information to those who need to know so that action can be taken.

[2]Control: a programme which is approved and managed or supervised by the Veterinary Authority of a country for the purpose of controlling a vector, pathogen or disease by specific measures applied throughout that country, or within a zone or compartment of that country.

Vaccines Available

Table 12: Currently available categories of NDV vaccines available, their modality of action and examples of vaccine formulations [1][2][3][26]

Category	Modality of Action	Example Vaccine Formulations
DNA vector vaccines	Carrier virus expressing one or more immunogenic NDV proteins (usually F and/or HN) induces an immune response against both NDV and the vector virus itself	Vaccinia virus (Meulemans, 1988), Fowlpox virus (Boursnell et al., 1990; Karaca et al., 1998; Olabode et al., 2010), Pigeonpox virus (Letellier et al., 1991), Herpesvirus of turkeys (Heckert et al., 1996; Morgan et al., 1992; Reddy et al., 1996), Marek's disease virus (Sakaguchi et al., 1998) and avian adeno-associated virus (Perozo et al., 2008)
Subunit vaccines	Expression of NDV proteins (usually F and/or HN)	Baculovirus vectors (Fukanoki et al., 2001; Lee et al., 2008; Mori et al., 1994; Nagy et al., 1991) or plants (Berinstein et al., 2005; Yang et al., 2007)
DNA vaccines, (plasmid)	DNA encoding relevant immunogenic NDV proteins	(Loke et al., 2005; Rajawat et al., 2008).
Reverse genetics vaccines	Modify the NDV genome and to develop NDV strains with new properties	Serological differentiation (DIVA vaccines (Mebatsion et al., 2002; Peeters et al., 2001) and the incorporation and expression of foreign genes, thereby making NDV itself a vaccine vector for application in poultry (Nakaya et al., 2001; 2010; Schroer et al., 2009; Steel et al., 2008) and other species, including primates (Dinapoli et al., 2007).

Category	Modality of Action	Example Vaccine Formulations
Live attenuated	Conventional egg passage attenuation ICPI < 0.4; live virus vaccines administered to birds by incorporation in the drinking water, delivered as a coarse spray (aerosol), or by intranasal or conjunctival instillation; some mesogenic strains are given by wing-web intradermal inoculation	Both thermostable heat tolerant selected Australian virus, strain I-2 isolated about 1990; live thermostabilised vaccine with D58 isolate from India; conventional temperature sensitive La Sota, F, Hitchner B1
Killed conventional vaccine	Inactivated virus prepared from allantoic fluid inactivated by the addition of formaldehyde or beta-propiolactone in oil emulsion; tend to be more expensive than live vaccines; application entails handling and injecting individual birds; administered intramuscularly or subcutaneously; each bird thus receives a standard dose; advantage of no subsequent spread of virus or adverse respiratory reactions; virulent and avirulent strains are used as seed virus; from a safety control perspective the use of the latter appears more suitable; much larger amount of antigen is required for immunization than for live virus vaccination (no virus multiplication)	Many commercial formulations (e.g. Intervet, Laprovet)

Commercial vaccines manufactured in Africa and Asia

Presented in Table 13 below is a list of vaccines licensed in the 20 selected countries is presented. Over 522 vaccines were reviewed.

Table 13: Commercial NDV vaccines manufactured in Africa and Asia.

Specific Vaccines and Formulation
AVI ND La Sota, water based delivery; Laprovet, Evervictory Ltd, Uganda.
*Avivax F Kenya Agricultural Research Institute [KARI]; F Type, La Sota strain; 0.1 ml/dose
Bio-Vac B1, Fatro, Italy (registered in Myanmar); 0.1 ml/dose
F Strain Indovax Private Ltd. India;
GlobiVac ND C131 Globion India Private Ltd.; 1 dose contains min. 106 EID 50 ND virus, Strain clone 13-1
*I2VAX Laboratoire National Vétérinaire [LANAVET]; Cameroon
*Kukustar vaccine Brentec Vaccines Limited Uganda; I2 thermostable vaccine;
La Sota Strain Indovax Private Ltd. India
Live B1 Hester Biosciences Ltd. India; Live attenuated; Intraocular, Intranasal, Subcutaneous, Oral, Drop eye
MEDIVAC ND CLONE-45 Medion Farma Jaya Indonesia; one dose (contains at least 10^7 EID50 ND virus) per chicken
MEDIVAC ND HITCHNER B1 45 Medion Farma Jaya Indonesia;

Specific Vaccines and Formulation
Mild Living Vaccine of Newcastle Disease (Clone-30 Strain) in oil emulsion; Qingdao Yebio Bioengineering Co. Ltd. China; 0.05 ml
*HB1, La Sota, thermostable-I2; Newcastle Disease National Veterinary Institute of Ethiopia;
Newcastle Disease Vaccine Living (La Sota Strain) B.P. (Vet.) Ventri Biologicals [Venkateshwara Hatcheries Private Ltd.] India
Ranikhet disease Vaccine F Institute of Animal Health and Veterinary Biologicals [Kerala]; India; *Chicks at one day of age.
*Ranikhet Disease Vaccine, Live, Lentogenic "F" Strain, I.P. (Vet.) BiO-MED Private Ltd.; Intranasal, intraocular, Oral, eye drop
*TAbic V.H. Clone (Tablet vaccine) Phibro Vaccines [ABIC Biological Laboratories] Spray method, Oral, Intraocular, eye drop; V.H. Clone, Lyophilized live vaccine in vials (Israel, Myanmar)
*TEMEVAC, Thermo-tolerant Newcastle Disease Vaccine Strain I-2 Tanzania Veterinary Laboratory Agency; Ocular
V.H. Phibro Vaccines [ABIC Biological Laboratories] India, Israel; Spray method, Oral, Drop eye, Intraocular
Vaksimune Clone, Vaksindo, Indonesia; ND Clone Spray method, Oral, Intraocular, Drop eye
Vaksimune NDHV; Vaksindo, Indonesia; Live Ulster attenuated
AVIVAC ND DELTAMUNE (Pty), Ltd. South Africa; Killed oil emulsion 0.5 ml/dose
Cevac Broiler ND K; Ceva Sante Animale; Oil emulsion 0.1 ml/dose (China, Indonesia, South Africa)
Encivax Indovax Private Ltd. India; Killed oil emulsion 0.5 ml/dose subcutaneous, intramuscular
GlobiVac NDK Globion India Private Ltd. India; Killed oil emulsion 0.5 ml/dose subcutaneous, intramuscular
Imopest (Gallimune ND) MCI Sante Animale [Merial] Ulster 2c Strain; Killed inactivated in oil emulsion; 0.3ml intramuscular injection; (China, Myanmar)

Specific Vaccines and Formulation
Inactivated Chick-ND Hester Biosciences Ltd. India; 0.5 ml subcutaneous; Formulated for chicks from 1-10 days of age.
ITA-NEW Laprovet, France, Uganda; 0.2-0.5 ml/dose subcutaneous or intramuscular; Additional information from Evervictory Ltd, Uganda
Jova Zeit 1,7 Jordan Bio-Industries Center (JOVAC) (Jordan, Ethiopia) Bivalent Killed ND/AI vaccine La Sota and H9N2
MEDIVAC ND-AI Emulsion Medion Farma Jaya Indonesia; Killed La Sota and H5 in oil emulsion; 0.2 ml per young chicken or 0.5 ml per adult chicken.
Mukteshwar Strain (R2B) Indovax Private Ltd. India; 0.5 ml/dose intramuscular or subcutaneous
Nectiv Phibro Vaccines [ABIC Biological Laboratories] Israel. (Licensed in India); V.H. strain; Chickens and turkeys. Dosage: 7-21 old chicks 0.3 ml; 21 day old chicks and older 0.5 ml. Oil emulsion.
Newcastle Disease Vaccine Living (R2B Strain) B.P. (Vet.) Ventri Biologicals [Venkateshwara Hatcheries Private Ltd.] India; oil emulsion; 0.5ml Intramuscular, Subcutaneous
newcastle influenza Avimex S.A. de C.V.; H5N2 La Sota mineral oil emulsion; 0.05 ml/dose subcutaneous (Mexico, Indonesia)
Nobivac ND Broiler MSD Animal Health [Intervet, Schering-Plough Animal Health, Merck Sharp & Dohme, Coopers Animal Health]; Killed oil emulsion; 0.1 ml/dose intramuscular subcutaneous in day old chicks
OL-VAC Fatro Italy, Myanmar; Mineral oil 0.5 ml/dose; Vaccination scheme: first dose at 18-20 days and second at 18-20 weeks.
*Vaksimune ND L Inaktif Vaksindo; Indonesia; Genotype VII, strain N018; oil emulsion
Newcastle disease, avian flu combined vaccine (H9,F strain, Lo Sota) [killed] Merial China subcutaneous injection from neck
Newcastle disease, avian flu combined vaccine (rLH5-6 strain) [live] Weke Biotechnology (the vaccine company supported by Harbin Veterinary Research Institute); 0.05ml nose drops or eye drops for each chicken and 0.2ml I.M. for each one

Commercial vaccines imported into Africa and Asia

Table 14: Newcastle disease commercial vaccines imported into Africa and Asia and the number of doses used annually 2012-2015

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
Burkina Faso							
Ethiopia							
Ivory Coast	Avi Nd La Sota+Ib		Hongrie	25 000 000			
	Avinew		France	605 000			
	Bronhipra		Espagne	400 000			
	Ceva Nd		Hongrie	650 000			
	Ceva New		Hongrie	7 000 000			
	Gallimune Nd E		France	10 000 000			
	Gumbopest		France	26 000			
	Hipraviar H120		Espagne	1 500 000			
	Hipraviar Clon H120		Espagne	1 200 000			
	Imopest		France	700 000			
	Inmugal		Espagne	5 000 000			

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	Itanew		Italie	600 000			
	Ita Nd		Hongrie	2 000 000			
	Izovac Hitchner B1 La Sota		Bresil/Italie	30 000 000			
Kenya				N/A	N/A	N/A	N/A
Madagascar							
Malawi	Lasota	Live Attenuated	Rsa	3,600,000	3,000,000	2,600,000	2,750,000
	Hitchner	Live Attenuated	Rsa	1,500,000	150,000	1,700,000	1,200,000
Mali	Itanew; B8l; Ceva Newl; Cevaunil; Imopest; Avinew; Gomboro Nd; Collimune	Hitchener B1; Lasota	France, Holland	21,900,000	21,200,000	19,800,000	20,000,000
Mozambique							
Rwanda			Belgium	2,210,000	1,800,000	1,500,000	
Senegal							
South Africa							

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
Tanzania		B1 And La Sota	Hungary		35		
Uganda		Lasota, Clon 30,VG/VA	Various	63,906,000	82,963,000	11,550,000	26,083,000
		Various	Various	35,287,000	28,550,000	9,229,000	13,520,000
		Various		48,000	75,000	30,000	10,000
Zambia	NA	B1	India	2,400,000	5,100,000	2,100,000	NA
	NA		Republic Of South Africa	2,100,000	-	3,100,000	NA
	NA	6/10	Republic Of South Africa	NA	81,000	NA	NA
	NA	La Sota	India	90,830,000	7,600,000	11,075,000	NA
	NA		Ireland		1,050,000		NA
	NA		Isreal	1,250,000			NA
	NA		Republic Of South Africa	25,392,500	21,987,200	23,761,000	NA
	NA		Egypt	500,000			NA
	NA		Spain	100,000			NA

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	NA		USA	500,000			
	NA	C131	Republic Of South Africa	1,450,000			NA
	NA	Clone 30	Republic Of South Africa	2,220,000	1,500,000		NA
	NA	VH	Republic Of South Africa	114,000			NA
	NA	Inactivated Virus	Republic Of South Africa	100,000			
	NA	Live Attenuated	Republic Of South Africa	64,000			
	NA	Not Available (NA)	Ireland	1,520,000			NA
	NA		Isreal	780,000	1,084,000	330	
	NA		Republic Of South Africa	15,694,500	22,798,500	9,868,000	
	NA		India	100,000			
Bangladesh	Lasota Vaccine	Lasota Strain	126,660,000	77,315,000	110,630,000	146,681,000	

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	ND Vaccine	Live And Killed(B1/F)	173,180,000	507,000,000	383,700,000	488,000,000	
India							
Nepal	Vir 220 ND / IB	Lasota H120	Israel	4,850,000	3,395,000	1,697,500	509,250
	Avinew	Newcastle VG/GA	France	1,000,000	700,000	350,000	105,000
	Biovac Lasota	Lasota	Italy	1,200,000	840,000	420,000	126,000
	Biovac Lasota H120	Lasota & Massachusetts H120	Italy	1,320,000	924,000	462,000	138,600
	Biovac NDV 6/10	NDV 6/10 Of ND Virus	Italy	1,000,000	700,000	350,000	105,000
	Bronki -L	Mass H120+Lasota	India	1,600,000	1,120,000	224,000	33,600
	DS ND-IB	B1 H120	Korea	9,000,000	6,300,000	3,150,000	945,000
	Encivax	Lasota	India	200,000	140,000	28,000	4,200
	Gallimune 403	ND-Ulster 2C,IB-Massachusse tts 41, IBD-	Italy	500,000	350,000	175,000	52,500

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
		VNJO, EO-S1133					
	Himmvac IB-ND Combined	H120+B1	Korea	4,000,000	2,800,000	1,400,000	420,000
	Himmvac Lasota	Lasota	Korea	11,075,000	7,752,500	3,876,250	1,162,875
	Himmvac ND+IB	Lasota H120	Korea	4,534	3,174	1,587	476
	IB -Olvac	Lasota+ Massachusets M41	Italy	225,000	157,500	78,750	23,625
	IB+Lasota	ND Lasota & Mass Type	India	200,000	140,000	28,000	4,200
	IB+ND	Massachusets H120+Lasota	India	600,000	420,000	84,000	12,600
	IBD Plus	Intermediate Plus	India	17,000,000	11,900,000	2,380,000	357,000
	IZO Vac Lasota	Lasota	Italy	2,000,000	1,400,000	700,000	210,000
	IZO Vac ND-IB	Lasota+ W2512	Italy	600,000	420,000	210,000	63,000
	IZO Vac 120 Clone	Lasota	Italy	1,800,000	1,260,000	630,000	189,000

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	IZO Vac 120-Lasota	Lasota, Madachusetts	Italy	15,000,000	10,500,000	5,250,000	1,575,000
	IZO Vac B1	B1	Italy	600,000	420,000	210,000	63,000
	IZO Vac Clone	Lasota	Italy	2,000,000	1,400,000	700,000	210,000
	IZO Vac ND+IB+IBD+Reo	Ulster M41, W2512, S1133	Italy	1,200,000	840,000	420,000	126,000
	IZOVAC B1	B1	Italy	1,000,000	700,000	350,000	105,000
	Izovac IB H120	Massachusetts	Italy	1,000,000	700,000	350,000	105,000
	Izovac Lasota	Lasota	Italy	1,500,000	1,050,000	525,000	157,500
	ND +IB+IBD	Lentogenic Lasota Mass Type IB Lukert	India	100,000	70,000	14,000	2,100
	ND B1	Lentogenic B1	India	7,700,000	5,390,000	1,078,000	161,700
	ND B1+IB	ND B1 Strain & Mass Type	India	100,000	70,000	14,000	2,100

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	ND IBD	Lentogenic Lasota Lukert Type	India	2,040,000	1,428,000	285,600	42,840
	ND Lasota	Lasota	India	18,050,000	12,635,000	2,527,000	379,050
	ND Lasota+Bronchitis Vac.	Lasota IB Massachusets (M41)	Singapore	300,000	210,000	105,000	31,500
	Nectiv Forte	VH Clone	Israel	500,000	350,000	175,000	52,500
	New Castle Bron Mass	Lasota IB Massachusets (M41)	Singapore	1,800,000	1,260,000	630,000	189,000
	Newcastl & Avian Infectious Bronchitis	Lasota & Mass Type	India	75,000	52,500	10,500	1,575
	Newcastle Disease Vac.	Lentogenic Lasota	India	2,760,000	1,932,000	386,400	57,960
	Newcastle Lasota+ Bron Mass Vac	Lasota IB+M-41	Korea	1,000,000	700,000	350,000	105,000
	Nobilis IB+ND	Inactivated IB M41, ND Clone 30 Virus	The Netherlands	144,000	100,800	50,400	15,120

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	Nobilis MA5+Clone 30	IB Ma5, ND Clone30	The Netherlands	6,400,000	4,480,000	2,240,000	672,000
	Nobilis ND Clone 30	ND Clone 30	The Netherlands	1,000,000	700,000	350,000	105,000
	Nobilis ND Clone 30	ND Clone 30	The Netherlands	1,000,000	700,000	350,000	105,000
	Nobilis ND Clone 30	ND Clone 30	The Netherlands	500,000	350,000	175,000	52,500
	Nobilis ND Clone 30	ND Clone 30	The Netherlands	1,000,000	700,000	350,000	105,000
	Nobilis ND Lasota	ND Lasota	The Netherlands	300,000	210,000	105,000	31,500
	Nobilis ND Lasota	ND Lasota	The Netherlands	500,000	350,000	175,000	52,500
	Nobilis ND Lasota	Lasota	The Netherlands	250,000	175,000	87,500	26,250
	Nobilis ND Lasota	Lasota	The Netherlands	250,000	175,000	87,500	26,250
	Nobilis ND Lasota	Lasota	The Netherlands	300,000	210,000	105,000	31,500

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	Nobilis ND Lasota	ND Lasota	The Netherlands	1,000,000	700,000	350,000	105,000
	Nobilis Newcavac	Inactivated ND Clone 30	The Netherlands	12,000	8,400	4,200	1,260
	Nobilis Newcavac	Inactivated ND Clone 30	The Netherlands	60,000	42,000	21,000	6,300
	Nobilis Newcavac	Inactivated ND Clone 30	The Netherlands	60,000	42,000	21,000	6,300
	Nobilis Reo+IB+G+ND	Inactivated IBV M41,NDV Clon 30,IBDV D78, Reo Virus Strain 1733 & 2408	The Netherlands	92,000	64,400	32,200	9,660
	OL Vac	Lasota Of ND Virus	Italy	54,000	37,800	18,900	5,670
	Olvac A+B+G	ND Lasota,IB M41,IBD Winterfield, EDS 76	Italy	18,000	12,600	6,300	1,890
	Olvac A+B+G	ND Lasota,IB M41,IBD	Italy	18,000	12,600	6,300	1,890

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
		Winterfield, EDS 76					
	Olvac A+B+G	ND Lasota,IB M41,IBD Winterfield, EDS 76	Italy	18,000	12,600	6,300	1,890
	Olvac A+B+G	ND Lasota,IB M41,IBD Winterfield 2512, EDS EDS76	Italy	18,000	12,600	6,300	1,890
	Olvac B+G+R	Lasota+Massachusetts M41+Winterfield2512 +S 1133 Of Reo Virus	Italy	1,500,000	1,050,000	525,000	157,500
	Poulshot Lasota	Newcastle Lasota	Korea	500,000	350,000	175,000	52,500
	Poulshot Lasota+IB	Lasota+ IB H120	Korea	1,000,000	700,000	350,000	105,000
	Poulshot Gumboro	Intermediate LZD 288 JAC3	Korea	1,000,000	700,000	350,000	105,000

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	Poulshot ING-Plus	IB M41& KM491,ND: Lasota IBD:CAG Intermediate	Korea	100,000	70,000	35,000	10,500
	Poulshot Lasota	Lasota	Korea	500,000	350,000	175,000	52,500
	Poulshot Lasota+IB	Lasota +IB H120	Korea	1,000,000	700,000	350,000	105,000
	Poulvac N+B	Lasota IB Massachusets (M41)	Singapore	30,000	21,000	10,500	3,150
	Poulvac N+B Vac	Lasotaib Massachusets (M41)	Singapore	20,000	14,000	7,000	2,100
	Poulvac N+B Vac	Lasotaib Massachusets (M41)	Singapore	30,000	21,000	10,500	3,150
	Poulvac N+B Vac	Lasotaib Massachusets (M41)	Singapore	30,000	21,000	10,500	3,150
	Poulvaci N+B	ND Lasota & Bronchitis Mass	Singapore	200,000	140,000	70,000	21,000

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	Pro Vac IBD	VMG 91	Singapore	800,000	560,000	280,000	84,000
	Pro Vac IBD	VMG 91	Singapore	3,500,000	2,450,000	1,225,000	367,500
	Pro Vac ND IB	Hitchner B1,IB H120	Singapore	1,000,000	700,000	350,000	105,000
	Pro Vac ND IB	Hitchner B1,IB H120	Singapore	1,000,000	700,000	350,000	105,000
	Pro Vac ND Lasota	Lasota	Singapore	850,000	595,000	297,500	89,250
	Pro Vac ND Lasota	Lasota	Singapore	3,500,000	2,450,000	1,225,000	367,500
	Pro Vac ND Lasota	Lasota	Singapore	800,000	560,000	280,000	84,000
	Pro Vac ND Lasota	Lasota	Singapore	2,000,000	1,400,000	700,000	210,000
	Quadractin	(VH+IB M41+MB+Re o S1133	Israel	2,000,000	1,400,000	700,000	210,000
	R2B	Mukteshwor	India	600,000	420,000	84,000	12,600
	R2B	R2B Mukteswar Virus Strain	India	500,000	350,000	70,000	10,500
	R2B	Mukteshwor	India	40,000	28,000	5,600	840

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
	R2B	Mukteshwor	India	400,000	280,000	56,000	8,400
	R2B	Mukteshwor	India	80,000	56,000	11,200	1,680
	R2B	Mukteshwor	India	400,000	280,000	56,000	8,400
	R2B	Mukteshwor	India	200,000	140,000	28,000	4,200
	Ranikhet	Lasota	India	17,000,000	11,900,000	2,380,000	357,000
	Ranikhet With Diluent	Lentogenic F I.P.	India	130,000	91,000	18,200	2,730
	Ranikhet F Strain	F Strain	India	36,500,000	25,550,000	5,110,000	766,500
	VH	VH Clone (Lentogenic)	Israel	800,000	560,000	280,000	84,000
	VH+ H120	VH+ H120	Israel	4,000,000	2,800,000	1,400,000	420,000
	Vir- 116 ND Lasota	Lasota	Israel	3,200,000	2,240,000	1,120,000	336,000
	Vir-106 –ND B1	Hitchner B1	Israel	13,640,000	9,548,000	4,774,000	1,432,200
	Virsin-116 ND Lasota	Lasota	Israel	2,500,000	1,750,000	875,000	262,500
	Vol Vac IBH+ND	Adino Virus Type 4+ Lasota	Germany	2,500,000	1,750,000	875,000	262,500

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
			Totals	816,058,534	162,220,474	58,792,487	15,405,971
Indonesia							
Myanmar	TABIC,Bio Vac, OL-VAC, Impoest	Clone 30 Lasota, 126 Strain, Ulster 2c,	USA (Israel), Italy, Spain, France	100,878,000	95,220,000	105,260,000	115,000
Vietnam			• Venkateshwara Hatcheries • Hester Biosiences Limited • Intervet • Boehringer Inhejhem Vet • Choongang Vaccine Laboratory • Daesung Microbiological Lab • P.T. Medion • Formosa Biomedical • Vaccines And Pharmaceuticals Sdn. Bhd				

Country	Name	Strain Or Type	Country Of Origin	Doses Imported 2015	Doses Imported 2014	Doses Imported 2013	Doses Imported 2012
			• Dodge Animal Health • Lohman Animal Health Gmbh • Schering-Plough Animal Health • Merial • Ceva Sante Animale/ Ceva-Phylaxia Veterinary Biologicals Co. Ltd. • Bestar Laboratories • Laboratories Hipra S.A. • Guangdong Dahuanong Animal Health Products				

Characteristics of Ideal Vaccine Candidates for Smallholders

The strategic objectives for an ideal vaccine and vaccination program include the following:

1. Live prime dose that is safe and non-reverting to virulent form after it has circulated in live poultry;
2. Thermostable for ease of use in smallholder setting;
3. Protective, long-lasting immunity resulting in reduced replication and transmission on a population basis;
4. Vaccine is matched with the genotype of circulating field strains, ideally using reverse genetics technology [8][14];
5. Can be delivered easily using simple and attainable field logistics;
6. Rapid onset and long duration of immunity;
7. Potential combination as part of a multivalent vaccine with other priority diseases for smallholders such as IBD based on country needs assessments.

Table 15: Target product profile.

Attribute	Minimum (currently available vaccine)	Ideal
Antigen	Standard replicating lentogenic B1, La Sota, Ulster, F, Clone line	Non-replicating reverse genetics engineered for field strain based on genotype of field strain
Indication for use	Prevention and control of NDV	Reduced replication and shedding of NDV
Recommended species	Chickens, turkeys, pigeons	Primarily chickens
Recommended dose	Range of 0.05 ml by topical application (live attenuated) to 0.5 for injectable	0.05 ml by topical application

Pharmaceutical form	Antigenic as La Sota strain but mild as B1 of Newcastle Disease virus field strain and pathotype	Thermostable, reverse genetics engineered La Sota or similar strain
Route of administration	Topical and injectable	Topical for ease of application
Regimen – primary vaccination	Topical preferable to injectable	Day old chick
Regimen – booster	Killed vaccine follows live prime dose at one day of age	4-6 months ideally based on village flock serological profile results
Epidemiological relevance and use for smallholders	Limited to live attenuated thermostable vaccines	Both live attenuated and reverse genetics thermostable vaccines
Recommended age at first vaccination	Day old chick or up to 3 weeks of age	Day old chicks
Onset of immunity	10 days (live) - 21 days (killed)	7 days ideally
Duration of immunity	Range of 3 weeks (live prime) to 4 months (booster);	4-6 months
Expected efficacy	65-85% field	Minimum of 80% within-flock (villages) protection; 90% among flocks (villages)
Expected safety	80%	99%
Withdrawal period	21-42 days	Less than 21 days
Special requirements for animals	Live attenuated – vaccinate all flock members to avoid reversion to virulence in unvaccinated poultry; Killed – injection tissue granulomas	Safe with no granulomas to remove as disincentive to vaccinate
Special requirements for persons	Live attenuated – prevent conjunctivitis in vaccine and poultry handlers Killed – tissue reaction or anaphylaxis	Safe and non-reactive
Package size	100-5,000 doses per bottle	100-500 doses per bottle
Price to end user	$0.04-$0.1	$0.01 - $0.05
Storage condition and shelf-life as packages for sale	Thermo-intolerant: Keep in cool dark place 2-8 degrees centigrade	Thermo-tolerant for 8 weeks

	Thermo-tolerant: 3-8 weeks away from ultraviolet light	
In-use stability	Live – unstable and mix with non-chlorinated water Killed – greater stability under proper storage and timely administration – prevent bacterial contamination	Live/Killed – unstable Reverse genetic vaccines – higher level of stability

Key Conclusions Related to Vaccination

Short-term Solutions: Live, attenuated and killed, inactivated NDV vaccines are effective, and can produce protective titers when applied properly. The first approach would be to 1) improve disease detection using rapid test kits; 2) improve reporting; 3) and optimize the access and delivery of vaccines in the field since it is a limiting gap regardless of the vaccine that is used. Thermostable vaccines currently are closest to the ideal vaccine for use in smallholder poultry. Proper delivery of vaccine to smallholder with community engagement is a key gap to overcome logistical challenges for the safe and effective delivery of vaccine.

Medium-term Solutions: 1) The further development of reverse genetics vaccines antigenically matched with the field strain genotype will optimize the immune response (level and duration of immunity) in typical currently available vaccine strains. Investment in the collection and molecular analysis of country-specific field strains will be required. 2) Improvement in diagnostic tests in vitro (cell culture) and rapid tests in the field will also be needed.

Long-term Solutions: There are two main needs: 1) Further refinement of a vaccination model multivalent, non-replicating, antigenically matched and epidemiologically appropriate; 2) Development of breed lines of native poultry with high levels of innate genetic resistance to further reduce replication and to increase vaccine efficacy. Needs assessments are recommended to assess the need for a multivalent NDV vaccine in combination with infectious bursal disease (IBD) vaccine or other priority poultry disease, which also result in significant losses in some regions.

Limitations

This monograph uses an evidence-based approach consulting primary referenced studies which summarize key points and considerations for undertaking successful vaccine development. Reporting bias presents a significant handicap for estimating country-based risk for Newcastle disease as explained under section 3. Reporting bias is due to: 1) habituation of poultry owners to the regular and persistent losses due to NDV since farmers themselves have learned to "live with" the disease; 2) lack of capacity and transparency from government officials; 3) lack of incentive to report (no compensation paid). It is common for village poultry owners to eat recently dead or sick poultry due to food scarcity. Community engagement is therefore a critical consideration for any vaccination initiative. In addition, the prevalence studies are likely more useful to develop vaccination strategies, however they must be evaluated carefully. Study design greatly affects the interpretation of the results and how to best apply the results for future vaccination planning and delivery.

Gaps in knowledge or capacity impacting strategic planning and effective implementation. The following gaps are highlighted in relation to vaccine development and sustainable field implementation of vaccination for Newcastle disease:

1. Lack of accurate information on reservoirs as well as NDV incidence and prevalence from farmers, including epidemiologically related semi-intensive poultry producers and the government services;
2. Limited genotype characterization of country-specific field strains of NDV.
3. Need for field based rapid test kits to detect the field strains since no field-based test kits are currently available;
4. Need to replace the SPF chicken challenge-based model with a cell line culture model in developing countries with laboratories lacking BSL-3 required to conduct challenge studies safely;
5. Systematic delivery and monitoring of vaccine use so that it is applied uniformly among members of smallholder village flocks. Interestingly, Dr. David Suarez indicated that in Tanzania, as the availability of I-2 vaccine decreased due to high demand, the vaccine distributors and vaccinators began diluting the vaccine while charging the same price. Results suffered, and owner compliance also declined. Thus, an effective monitoring program of vaccine use is needed to avoid these issues;
6. Wider application of safe, non-replicating NDV vaccines at the interface of commercial and smallholder sectors where spillover can occur.

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